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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2.

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADO
NEWS	4	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	5	MAR 02	GBFULL: New full-text patent database on STN
NEWS	6	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	9	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	10	MAR 22	PATDPASPC - New patent database available
NEWS	11	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	12	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	13	APR 04	EMBASE - Database reloaded and enhanced
NEWS	14	APR 18	New CAS Information Use Policies available online
NEWS	15	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAPLUS and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAPLUS
NEWS	17	MAY 23	GBFULL enhanced with patent drawing images
NEWS	18	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	19	JUN 06	The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available
NEWS	20	JUN 13	RUSSIAPAT: New full-text patent database on STN
NEWS	21	JUN 13	FRFULL enhanced with patent drawing images
NEWS	22	JUN 27	MARPAT displays enhanced with expanded G-group definitions and text labels
NEWS	23	JUL 01	MEDICONF removed from STN
NEWS	24	JUL 07	STN Patent Forums to be held in July 2005
NEWS	25	JUL 13	SCISEARCH reloaded
NEWS	26	JUL 20	Powerful new interactive analysis and visualization software, STN AnaVist, now available
NEWS EXPRESS			JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS INTER			General Internet Information
NEWS LOGIN			Welcome Banner and News Items.
NEWS PHONE			Direct Dial and Telecommunication Network Access to STN
NEWS WWW			CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

\*ENCOMPPAT - EnCompass Patent File 1964-present (Supporters)  
\*ENCOMPPAT2 - EnCompass Patent File 1964-Present (Non-Supporters)

\* The files listed above are temporarily unavailable.

FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005

=> file medline	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

FILE LAST UPDATED: 23 JUL 2005 (20050723/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s WNT
      3897 WNT
      336 WNTS
L1      3942 WNT
      (WNT OR WNTS)

=> s l1 (S) antagon?
      518406 ANTAGON?
L2      244 L1 (S) ANTAGON?

=> s osteo? or bone
      211167 OSTEO?
      424243 BONE
      91740 BONES
      446342 BONE
      (BONE OR BONES)
L3      553450 OSTEO? OR BONE

=> s l3 and l2
L4      70 L3 AND L2

=> s multiple myeloma
      445180 MULTIPLE
```

3940 MULTIPLES  
446855 MULTIPLE  
(MULTIPLE OR MULTIPLES)  
30767 MYELOMA  
763 MYELOMAS  
31029 MYELOMA  
(MYELOMA OR MYELOMAS)  
L5 22597 MULTIPLE MYELOMA  
(MULTIPLE(W)MYELOMA)

=> s l5 and l4

L6 1 L5 AND L4

=> d ibib 1

L6 ANSWER 1 OF 1 MEDLINE on STN  
ACCESSION NUMBER: 2003612654 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14695408  
TITLE: The role of the Wnt-signaling antagonist  
DKK1 in the development of osteolytic lesions in  
multiple myeloma.  
COMMENT: Comment in: N Engl J Med. 2003 Dec 25;349(26):2479-80.  
PubMed ID: 14695406  
Comment in: N Engl J Med. 2004 Apr 1;350(14):1464-6; author  
reply 1464-6. PubMed ID: 15070800  
Comment in: N Engl J Med. 2004 Apr 1;350(14):1464-6; author  
reply 1464-6. PubMed ID: 15074002  
Comment in: N Engl J Med. 2004 Apr 1;350(14):1464-6; author  
reply 1464-6. PubMed ID: 15074001  
Comment in: N Engl J Med. 2004 Jul 8;351(2):197-8. PubMed  
ID: 15247367  
AUTHOR: Tian Erming; Zhan Fenghuang; Walker Ronald; Rasmussen Erik;  
Ma Yupo; Barlogie Bart; Shaughnessy John D Jr  
CORPORATE SOURCE: Donna D. and Donald M. Lambert Laboratory of Myeloma  
Genetics, Myeloma Institute for Research and Therapy,  
College of Medicine, University of Arkansas for Medical  
Sciences, Little Rock 72205, USA.  
CONTRACT NUMBER: CA55819 (NCI)  
CA97513 (NCI)  
SOURCE: New England journal of medicine, (2003 Dec 25) 349 (26)  
2483-94.  
Journal code: 0255562. ISSN: 1533-4406.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200401  
ENTRY DATE: Entered STN: 20031230  
Last Updated on STN: 20040107  
Entered Medline: 20040106

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
L2 244 S L1 (S) ANTAGON?  
L3 553450 S OSTEO? OR BONE  
L4 70 S L3 AND L2  
L5 22597 S MULTIPLE MYELOMA  
L6 1 S L5 AND L4

=> s l2 and l5

L7 1 L2 AND L5

=> s myeloma

30767 MYELOMA

763 MYELOMAS

L8 31029 MYELOMA

(MYELOMA OR MYELOMAS)

=> s l8 and l2

L9 1 L8 AND L2

=> s l1 and l3

L10 451 L1 AND L3

=> s l10 and l5

L11 7 L10 AND L5

=> s l11 not py>2002

1489868 PY>2002

L12 1 L11 NOT PY>2002

=> d ibib

L12 ANSWER 1 OF 1 MEDLINE on STN

ACCESSION NUMBER: 2001420323 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11468178

TITLE: Identifying intercellular signaling genes expressed in malignant plasma cells by using complementary DNA arrays.

AUTHOR: De Vos J; Couderc G; Tarte K; Jourdan M; Requirand G;

Delteil M C; Rossi J F; Mechti N; Klein B

CORPORATE SOURCE: INSERM U475, Unit for Cellular Therapy, CHU Montpellier, 99 Rue Puech Villa, 34197 Montpellier Cedex 5, France.

SOURCE: Blood, (2001 Aug 1) 98 (3) 771-80.

Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200109

ENTRY DATE: Entered STN: 20010917

Last Updated on STN: 20010917

Entered Medline: 20010913

=> d kwic

L12 ANSWER 1 OF 1 MEDLINE on STN

AB In multiple myeloma (MM), the growth of primary plasma cells depends not only on interleukin-6 (IL-6), but also on additional unidentified signals delivered by the bone marrow environment. Using Atlas complementary DNA (cDNA) arrays comprising 268 genes coding for intercellular signaling molecules, this study identified genes. . . . receptor (TR) that is linked to HB-EGF and syndecan-1 processing and to cell invasion, chemokine receptors CCR1 and CCR2, the Wnt pathway actor Frizzled-related protein (FRZB), and the Notch receptor ligand Jagged 2. These data, obtained with the Atlas cDNA array, . . .

CT B-Lymphocytes: ME, metabolism

Cell Division: DE, drug effects

Epidermal Growth Factor: ME, metabolism

Flow Cytometry

Gene Expression: GE, genetics

Humans

Multiple Myeloma: GE, genetics

\*Multiple Myeloma: ME, metabolism

Multiple Myeloma: PA, pathology

Neoplasm Proteins: GE, genetics  
Neoplasm Proteins: ME, metabolism  
\*Oligonucleotide Array Sequence Analysis: MT, methods  
\*Plasma Cells:.. . .

```
=> s (dickkopf () 1) or (DKK () 1)
      85 DICKKOPF
      8 DICKKOPFS
      90 DICKKOPF
        (DICKKOPF OR DICKKOPFS)
3513889 1
      49 DICKKOPF (W) 1
      119 DKK
        9 DKKS
      121 DKK
        (DKK OR DKKS)
3513889 1
      44 DKK (W) 1
L13      70 (DICKKOPF (W) 1) OR (DKK (W) 1)
```

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

```
L1      3942 S WNT
L2      244 S L1 (S) ANTAGON?
L3      553450 S OSTEO? OR BONE
L4      70 S L3 AND L2
L5      22597 S MULTIPLE MYELOMA
L6      1 S L5 AND L4
L7      1 S L2 AND L5
L8      31029 S MYELOMA
L9      1 S L8 AND L2
L10     451 S L1 AND L3
L11     7 S L10 AND L5
L12     1 S L11 NOT PY>2002
L13     70 S (DICKKOPF () 1) OR (DKK () 1)
```

```
=> s l13 and l11
L14     2 L13 AND L11
```

=> d ibib 1-2

```
L14 ANSWER 1 OF 2      MEDLINE on STN
ACCESSION NUMBER:      2005314981      IN-PROCESS
DOCUMENT NUMBER:       PubMed ID: 15965110
TITLE:                 How wnt signaling affects bone repair
                        by mesenchymal stem cells from the bone marrow.
AUTHOR:                 Gregory Carl A; Gunn William G; Reyes Emigdio; Smolarz
                        Angela J; Munoz James; Spees Jeffrey L; Prockop Darwin J
CORPORATE SOURCE:       Center for Gene Therapy, Tulane University Health Sciences
                        Center, 1430 Tulane Avenue, New Orleans, LA 70112..
                        ca_gregory@hotmail.com
SOURCE:                 Annals of the New York Academy of Sciences, (2005 May) 1049
                        97-106.
                        Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY:           United States
DOCUMENT TYPE:           Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:               English
FILE SEGMENT:           NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED;
                        Priority Journals
ENTRY DATE:             Entered STN: 20050621
                        Last Updated on STN: 20050621
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L14 ANSWER 2 OF 2 MEDLINE on STN  
 ACCESSION NUMBER: 2003612654 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 14695408  
 TITLE: The role of the Wnt-signaling antagonist DKK1 in the development of osteolytic lesions in multiple myeloma.  
 COMMENT: Comment in: N Engl J Med. 2003 Dec 25;349(26):2479-80. PubMed ID: 14695406  
 Comment in: N Engl J Med. 2004 Apr 1;350(14):1464-6; author reply 1464-6. PubMed ID: 15070800  
 Comment in: N Engl J Med. 2004 Apr 1;350(14):1464-6; author reply 1464-6. PubMed ID: 15074002  
 Comment in: N Engl J Med. 2004 Apr 1;350(14):1464-6; author reply 1464-6. PubMed ID: 15074001  
 Comment in: N Engl J Med. 2004 Jul 8;351(2):197-8. PubMed ID: 15247367  
 AUTHOR: Tian Erming; Zhan Fenghuang; Walker Ronald; Rasmussen Erik; Ma Yupo; Barlogie Bart; Shaughnessy John D Jr  
 CORPORATE SOURCE: Donna D. and Donald M. Lambert Laboratory of Myeloma Genetics, Myeloma Institute for Research and Therapy, College of Medicine, University of Arkansas for Medical Sciences, Little Rock 72205, USA.  
 CONTRACT NUMBER: CA55819 (NCI)  
 CA97513 (NCI)  
 SOURCE: New England journal of medicine, (2003 Dec 25) 349 (26) 2483-94.  
 Journal code: 0255562. ISSN: 1533-4406.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 200401  
 ENTRY DATE: Entered STN: 20031230  
 Last Updated on STN: 20040107  
 Entered Medline: 20040106

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
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 L6 1 S L5 AND L4  
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 L8 31029 S MYELOMA  
 L9 1 S L8 AND L2  
 L10 451 S L1 AND L3  
 L11 7 S L10 AND L5  
 L12 1 S L11 NOT PY>2002  
 L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
 L14 2 S L13 AND L11

=> d ibib kwic l12

L12 ANSWER 1 OF 1 MEDLINE on STN  
 ACCESSION NUMBER: 2001420323 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11468178  
 TITLE: Identifying intercellular signaling genes expressed in malignant plasma cells by using complementary DNA arrays.

AUTHOR: De Vos J; Couderc G; Tarte K; Jourdan M; Requirand G;  
 Delteil M C; Rossi J F; Mechti N; Klein B  
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 SOURCE: Blood, (2001 Aug 1) 98 (3) 771-80.  
 Journal code: 7603509. ISSN: 0006-4971.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 200109  
 ENTRY DATE: Entered STN: 20010917  
 Last Updated on STN: 20010917  
 Entered Medline: 20010913

AB In multiple myeloma (MM), the growth of primary plasma  
 cells depends not only on interleukin-6 (IL-6), but also on additional  
 unidentified signals delivered by the bone marrow environment.  
 Using Atlas complementary DNA (cDNA) arrays comprising 268 genes coding  
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 receptor (TR) that is linked to HB-EGF and syndecan-1 processing and to  
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 pathway actor Frizzled-related protein (FRZB), and the Notch receptor  
 ligand Jagged 2. These data, obtained with the Atlas cDNA array, . . .  
 CT B-Lymphocytes: ME, metabolism  
 Cell Division: DE, drug effects  
 Epidermal Growth Factor: ME, metabolism  
 Flow Cytometry  
 Gene Expression: GE, genetics  
 Humans  
 Multiple Myeloma: GE, genetics  
 \*Multiple Myeloma: ME, metabolism  
 Multiple Myeloma: PA, pathology  
 Neoplasm Proteins: GE, genetics  
 Neoplasm Proteins: ME, metabolism  
 \*Oligonucleotide Array Sequence Analysis: MT, methods  
 \*Plasma Cells: . . .

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
 L2 244 S L1 (S) ANTAGON?  
 L3 553450 S OSTEO? OR BONE  
 L4 70 S L3 AND L2  
 L5 22597 S MULTIPLE MYELOMA  
 L6 1 S L5 AND L4  
 L7 1 S L2 AND L5  
 L8 31029 S MYELOMA  
 L9 1 S L8 AND L2  
 L10 451 S L1 AND L3  
 L11 7 S L10 AND L5  
 L12 1 S L11 NOT PY>2002  
 L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
 L14 2 S L13 AND L11

=> s 113 and 13.

L15 19 L13 AND L3

=> s 115 and express?

932565 EXPRESS?

L16 14 L15 AND EXPRESS?

=> s l16 not py>2002  
1489868 PY>2002  
L17 6 L16 NOT PY>2002

=> d ibib 1-3

L17 ANSWER 1 OF 6 MEDLINE on STN  
ACCESSION NUMBER: 2002693855 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12455632  
TITLE: Bmp, Fgf and Wnt signalling in programmed cell death and  
chondrogenesis during vertebrate limb development: the role  
of Dickkopf-1.  
AUTHOR: Grotewold Lars; Ruther Ulrich  
CORPORATE SOURCE: Institut fur Entwicklungs- und Molekularbiologie der Tiere  
(EMT), Heinrich-Heine-Universitat, Dusseldorf, Germany.  
SOURCE: International journal of developmental biology, (2002) 46  
(7) 943-7.  
Journal code: 8917470. ISSN: 0214-6282.  
PUB. COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200306  
ENTRY DATE: Entered STN: 20021214  
Last Updated on STN: 20030619  
Entered Medline: 20030618

L17 ANSWER 2 OF 6 MEDLINE on STN  
ACCESSION NUMBER: 2002280313 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12021176  
TITLE: Global gene profiling in human endometrium during the  
window of implantation.  
AUTHOR: Kao L C; Tulac S; Lobo S; Imani B; Yang J P; Germeyer A;  
Osteen K; Taylor R N; Lessey B A; Giudice L C  
CORPORATE SOURCE: Department of Gynecology and Obstetrics, Stanford  
University, Stanford, California 94305, USA.  
CONTRACT NUMBER: U54 HD31398 (NICHD)  
SOURCE: Endocrinology, (2002 Jun) 143 (6) 2119-38.  
Journal code: 0375040. ISSN: 0013-7227.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200206  
ENTRY DATE: Entered STN: 20020522  
Last Updated on STN: 20020619  
Entered Medline: 20020618

L17 ANSWER 3 OF 6 MEDLINE on STN  
ACCESSION NUMBER: 2002131765 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11867524  
TITLE: The Wnt antagonist Dickkopf-1 is  
regulated by Bmp signaling and c-Jun and modulates  
programmed cell death.  
AUTHOR: Grotewold Lars; Ruther Ulrich  
CORPORATE SOURCE: Entwicklungs- und Molekularbiologie der Tiere,  
Heinrich-Heine Universitat, D-40225 Dusseldorf, Germany..  
lars.grotewold@uni-duesseldorf.de  
SOURCE: EMBO journal, (2002 Mar 1) 21 (5) 966-75.  
Journal code: 8208664. ISSN: 0261-4189.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200205



ENTRY DATE: Entered STN: 20020228  
Last Updated on STN: 20020515  
Entered Medline: 20020514

=> d ibib 4-6

L17 ANSWER 4 OF 6 MEDLINE on STN  
ACCESSION NUMBER: 2001447406 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11291860  
TITLE: The role of the homeodomain protein Bozozok in zebrafish axis formation.  
AUTHOR: Solnica-Krezel L; Driever W  
CORPORATE SOURCE: Department of Molecular Biology, Vanderbilt University, Nashville, Tennessee 37235, USA.. lilianna.solnica-krezel@vanderbilt.edu  
SOURCE: International journal of developmental biology, (2001) 45 (1) 299-310.  
Journal code: 8917470. ISSN: 0214-6282.  
PUB. COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

L17 ANSWER 5 OF 6 MEDLINE on STN  
ACCESSION NUMBER: 2001150174 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11159911  
TITLE: Wnt antagonism initiates cardiogenesis in Xenopus laevis.  
AUTHOR: Schneider V A; Mercola M  
CORPORATE SOURCE: Department of Cell Biology, Harvard Medical School, Boston, Massachusetts 02115, USA.  
CONTRACT NUMBER: R01 HL59502 (NHLBI)  
SOURCE: Genes & development, (2001 Feb 1) 15 (3) 304-15.  
Journal code: 8711660. ISSN: 0890-9369.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200103  
ENTRY DATE: Entered STN: 20010404  
Last Updated on STN: 20010404  
Entered Medline: 20010315

L17 ANSWER 6 OF 6 MEDLINE on STN  
ACCESSION NUMBER: 1999425169 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10495270  
TITLE: Dickkopf genes are co-ordinately expressed in mesodermal lineages.  
AUTHOR: Monaghan A P; Kioschis P; Wu W; Zuniga A; Bock D; Poustka A; Delius H; Niehrs C  
CORPORATE SOURCE: Division of Molecular Biology of the Cell I, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120, Heidelberg, Germany.  
SOURCE: Mechanisms of development, (1999 Sep) 87 (1-2) 45-56.  
Journal code: 9101218. ISSN: 0925-4773.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AJ243963; GENBANK-AJ243964  
ENTRY MONTH: 200003

ENTRY DATE: Entered STN: 20000327  
Last Updated on STN: 20000327  
Entered Medline: 20000316

=> d kwic 6

L17 ANSWER 6 OF 6 MEDLINE on STN  
TI Dickkopf genes are co-ordinately expressed in mesodermal lineages.  
AB Dickkopf-1 (dkk-1) is member of a novel family of secreted proteins and functions in head induction during Xenopus embryogenesis, acting as a . . . of two additional murine members of the dkk family, dkk-2 and dkk-3; and (2) analysis of adult and embryonic gene expression of mouse dkk-1,-2, and -3, Xenopus dkk-1 as well as chicken dkk-3. Comparative developmental analyses of the dkk-1, dkk-2 and dkk-3 in mice indicate that these genes are both temporally and spatially regulated. They define overlapping deep domains in mesenchymal lineages suggesting a co-ordinated mode of action. All dkks show distinct and elevated expression patterns in tissues that mediate epithelial- mesenchyme transformations suggesting that they may participate in heart, tooth, hair and whisker follicle, limb and bone induction. In the limb buds expression of these genes are found in regions of programmed cell death. In a given organ, dkk-1 tends to be the earliest member expressed . Comparison with Xenopus dkk-1 and chicken dkk-3 shows evolutionarily conserved expression patterns. Our observations indicate that dkk genes constitute a new family of secreted proteins that may mediate inductive interactions between. . .  
CT Amino Acid Sequence  
Animals  
Ectoderm: ME, metabolism  
Epithelial Cells: ME, metabolism  
\*Gene Expression Regulation, Developmental  
In Situ Hybridization  
\*Mesoderm: ME, metabolism  
Mice  
Molecular Sequence Data  
\*Proteins: GE, genetics  
\*Proteins: ME, metabolism  
Reverse. . .

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.44	5.65

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005  
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FILE COVERS 1907 - 25 Jul 2005 VOL 143 ISS 5  
FILE LAST UPDATED: 24 Jul 2005 (20050724/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> s WNT

4331 WNT  
330 WNTS  
L18 4365 WNT  
(WNT OR WNTS)

=> s l1 (S) antagon?

4331 WNT  
330 WNTS  
4365 WNT  
(WNT OR WNTS)  
270850 ANTAGON?  
L19 273 L1 (S) ANTAGON?

=> s l18 (S) antagon?

270850 ANTAGON?  
L20 273 L18 (S) ANTAGON?

=> s myeloma

16718 MYELOMA  
557 MYELOMAS  
L21 16913 MYELOMA  
(MYELOMA OR MYELOMAS)

=> s l20 and l21

L22 5 L20 AND L21

=> d ibib 1-3

L22 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:450819 CAPLUS

DOCUMENT NUMBER: 142:461611

TITLE: Diagnosis, prognosis and identification of potential  
therapeutic targets of multiple myeloma  
based on gene expression profiling

INVENTOR(S): Shaughnessy, John D.; Barlogie, Bart; Zhan, Fenghuang  
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 80 pp., Cont.-in-part of U.S.  
Ser. No. 454,263.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005112630	A1	20050526	US 2004-931780	20040901
US 2003175753	A1	20030918	US 2002-289746	20021107
US 2003232364	A1	20031218	US 2003-409004	20030408
US 2004009523	A1	20040115	US 2003-454263	20030604
PRIORITY APPLN. INFO.:			US 2001-348238P	P 20011107
			US 2002-355386P	P 20020208
			US 2002-403075P	P 20020813
			US 2002-289746	A2 20021107
			US 2003-409004	A2 20030408
			US 2003-454263	A2 20030604

L22 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:992468 CAPLUS  
 DOCUMENT NUMBER: 142:371352  
 TITLE: Wnt signaling antagonist DKK1 in  
 the development of osteolytic lesion in multiple  
 myeloma  
 AUTHOR(S): Sato, Kanji  
 CORPORATE SOURCE: Institute of Clinical Endocrinology, Tokyo  
 Women's Medical University, Tokyo, 162-8666,  
 Japan  
 SOURCE: Ketsueki, Shuyoka (2004), 49(2), 166-170  
 CODEN: KETSBI; ISSN: 0915-8529  
 PUBLISHER: Kagaku Hyoronsha  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: Japanese

L22 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:515641 CAPLUS  
 DOCUMENT NUMBER: 141:52350  
 TITLE: Expression of genes DKK1 and FRZB as molecular  
 determinants of myeloma bone disease and  
 transcription regulation for treatment thereof  
 INVENTOR(S): Shaughnessy, John D.  
 PATENT ASSIGNEE(S): The Board of Trustees of the University of Arkansas,  
 USA  
 SOURCE: PCT Int. Appl., 89 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004053063	A2	20040624	WO 2003-US38372	20031204
WO 2004053063	A3	20041125		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004137489	A1	20040715	US 2003-727461	20031204
PRIORITY APPLN. INFO.:			US 2002-431040P	P 20021205

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L22 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:40999 CAPLUS  
 DOCUMENT NUMBER: 140:109553  
 TITLE: Diagnosis, prognosis and identification of potential  
 therapeutic targets of multiple myeloma  
 based on gene expression profiling  
 INVENTOR(S): Shaughnessy, John D.; Zhan, Fenghuang; Barlogie, Bart  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-part of U.S.  
 Ser. No. 409,004.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009523	A1	20040115	US 2003-454263	20030604
US 2003175753	A1	20030918	US 2002-289746	20021107
US 2003232364	A1	20031218	US 2003-409004	20030408
US 2005112630	A1	20050526	US 2004-931780	20040901
PRIORITY APPLN. INFO.:			US 2001-348238P	P 20011107
			US 2002-355386P	P 20020208
			US 2002-403075P	P 20020813
			US 2002-289746	A2 20021107
			US 2003-409004	A2 20030408
			US 2003-454263	A2 20030604

L22 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1011522 CAPLUS

DOCUMENT NUMBER: 140:126264

TITLE: The role of the Wnt-signaling  
antagonist DKK1 in the development of  
osteolytic lesions in multiple myeloma

AUTHOR(S): Tian, Erming; Zhan, Fenghuang; Walker, Ronald;  
Rasmussen, Erik; Ma, Yupo; Barlogie, Bart;  
Shaughnessy, John D., Jr.

CORPORATE SOURCE: Donna D. and Donald M. Lambert Laboratory of Myeloma  
Genetics, Myeloma Institute for Research and Therapy,  
College of Medicine, University of Arkansas for  
Medical Sciences, Little Rock, AR, USA

SOURCE: New England Journal of Medicine (2003), 349(26),  
2483-2494

CODEN: NEJMAG; ISSN: 0028-4793

PUBLISHER: Massachusetts Medical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s (dickkopf (), 1) or (DKK () 1)

175 DICKKOPF

8 DICKKOPFS

177 DICKKOPF

(DICKKOPF OR DICKKOPFS)

8339167 1

104 DICKKOPF (W) 1

123 DKK

11 DKKS

124 DKK

(DKK OR DKKS)

8339167 1

58 DKK (W) 1

L23 123 (DICKKOPF (W) 1) OR (DKK (W) 1)

=> s dickkopf-1 or DKK1

175 DICKKOPF

8 DICKKOPFS

177 DICKKOPF

(DICKKOPF OR DICKKOPFS)

8339167 1

104 DICKKOPF-1

(DICKKOPF(W)1)

98 DKK1

L24 155 DICKKOPF-1 OR DKK1

=> s l23 or l24  
L25 170 L23 OR L24

=> s osteo?  
L26 61795 OSTEO?

=> s l26 and l25  
L27 32 L26 AND L25

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
L2 244 S L1 (S) ANTAGON?  
L3 553450 S OSTEO? OR BONE  
L4 70 S L3 AND L2  
L5 22597 S MULTIPLE MYELOMA  
L6 1 S L5 AND L4  
L7 1 S L2 AND L5  
L8 31029 S MYELOMA  
L9 1 S L8 AND L2  
L10 451 S L1 AND L3  
L11 7 S L10 AND L5  
L12 1 S L11 NOT PY>2002  
L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
L14 2 S L13 AND L11  
L15 19 S L13 AND L3  
L16 14 S L15 AND EXPRESS?  
L17 6 S L16 NOT PY>2002

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005

L18 4365 S WNT  
L19 273 S L1 (S) ANTAGON?  
L20 273 S L18 (S) ANTAGON?  
L21 16913 S MYELOMA  
L22 5 S L20 AND L21  
L23 123 S (DICKKOPF () 1) OR (DKK () 1)  
L24 155 S DICKKOPF-1 OR DKK1  
L25 170 S L23 OR L24  
L26 61795 S OSTEO?  
L27 32 S L26 AND L25

=> s l27 and l21  
L28 7 L27 AND L21

=> d ibib 1-4

L28 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:450819 CAPLUS

DOCUMENT NUMBER: 142:461611

TITLE: Diagnosis, prognosis and identification of potential  
therapeutic targets of multiple myeloma  
based on gene expression profiling

INVENTOR(S): Shaughnessy, John D.; Barlogie, Bart; Zhan, Fenghuang

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 80 pp., Cont.-in-part of U.S.  
Ser. No. 454,263.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005112630	A1	20050526	US 2004-931780	20040901
US 2003175753	A1	20030918	US 2002-289746	20021107
US 2003232364	A1	20031218	US 2003-409004	20030408
US 2004009523	A1	20040115	US 2003-454263	20030604
PRIORITY APPLN. INFO.:			US 2001-348238P	P 20011107
			US 2002-355386P	P 20020208
			US 2002-403075P	P 20020813
			US 2002-289746	A2 20021107
			US 2003-409004	A2 20030408
			US 2003-454263	A2 20030604

L28 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2005:348815 CAPLUS  
 DOCUMENT NUMBER: 142:397651  
 TITLE: Inhibitors of protein Dickkopf-1  
 for treating osteolytic lesions in multiple  
 myeloma and enhancing osteogenesis  
 INVENTOR(S): Prockop, Darwin; Gregory, Carl; Gunn, William  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 84 pp., Cont.-in-part of U.S.  
 Ser. No. 830,352, abandoned.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005084494	A1	20050421	US 2004-839515	20040505
US 2004235166	A1	20041125	US 2003-442506	20030521
PRIORITY APPLN. INFO.:			US 2003-442506	A2 20030521
			US 2004-830352	B2 20040422

L28 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:992468 CAPLUS  
 DOCUMENT NUMBER: 142:371352  
 TITLE: Wnt signaling antagonist DKK1 in the  
 development of osteolytic lesion in multiple  
 myeloma  
 AUTHOR(S): Sato, Kanji  
 CORPORATE SOURCE: Institute of Clinical Endocrinology, Tokyo  
 Women's Medical University, Tokyo, 162-8666,  
 Japan  
 SOURCE: Ketsueki, Shuyoka (2004), 49(2), 166-170  
 CODEN: KETSBI; ISSN: 0915-8529  
 PUBLISHER: Kagaku Hyoronsha  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: Japanese

L28 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:515641 CAPLUS  
 DOCUMENT NUMBER: 141:52350  
 TITLE: Expression of genes DKK1 and FRZB as  
 molecular determinants of myeloma bone  
 disease and transcription regulation for treatment  
 thereof  
 INVENTOR(S): Shaughnessy, John D.  
 PATENT ASSIGNEE(S): The Board of Trustees of the University of Arkansas,  
 USA  
 SOURCE: PCT Int. Appl., 89 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent

LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004053063	A2	20040624	WO 2003-US38372	20031204
WO 2004053063	A3	20041125		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004137489	A1	20040715	US 2003-727461	20031204
PRIORITY APPLN. INFO.:			US 2002-431040P	P 20021205

=> d ibib 5-7

L28 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:504577 CAPLUS  
DOCUMENT NUMBER: 141:219048  
TITLE: Activation mechanism of osteoclasts  
AUTHOR(S): Sato, Kanji  
CORPORATE SOURCE: Dep. of Medicine II, Tokyo Women's Medical University, Tokyo, 162-8666, Japan  
SOURCE: Ketsueki, Shuyoka (2004), 48(3), 274-280  
CODEN: KETSBI; ISSN: 0915-8529  
PUBLISHER: Kagaku Hyoronsha  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

L28 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:40999 CAPLUS  
DOCUMENT NUMBER: 140:109553  
TITLE: Diagnosis, prognosis and identification of potential therapeutic targets of multiple myeloma based on gene expression profiling  
INVENTOR(S): Shaughnessy, John D.; Zhan, Fenghuang; Barlogie, Bart  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-part of U.S. Ser. No. 409,004.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009523	A1	20040115	US 2003-454263	20030604
US 2003175753	A1	20030918	US 2002-289746	20021107
US 2003232364	A1	20031218	US 2003-409004	20030408
US 2005112630	A1	20050526	US 2004-931780	20040901
PRIORITY APPLN. INFO.:			US 2001-348238P	P 20011107
			US 2002-355386P	P 20020208
			US 2002-403075P	P 20020813
			US 2002-289746	A2 20021107
			US 2003-409004	A2 20030408
			US 2003-454263	A2 20030604



L28 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:1011522 CAPLUS  
 DOCUMENT NUMBER: 140:126264  
 TITLE: The role of the Wnt-signaling antagonist DKK1  
 in the development of osteolytic lesions in  
 multiple myeloma  
 AUTHOR(S): Tian, Erming; Zhan, Fenghuang; Walker, Ronald;  
 Rasmussen, Erik; Ma, Yupo; Barlogie, Bart;  
 Shaughnessy, John D., Jr.  
 CORPORATE SOURCE: Donna D. and Donald M. Lambert Laboratory of Myeloma  
 Genetics, Myeloma Institute for Research and Therapy,  
 College of Medicine, University of Arkansas for  
 Medical Sciences, Little Rock, AR, USA  
 SOURCE: New England Journal of Medicine (2003), 349(26),  
 2483-2494  
 CODEN: NEJMAG; ISSN: 0028-4793  
 PUBLISHER: Massachusetts Medical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file pctfull		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	40.47	46.12

FILE 'PCTFULL' ENTERED AT 13:10:21 ON 25 JUL 2005  
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FILE LAST UPDATED: 19 JUL 2005 <20050719/UP>  
 MOST RECENT UPDATE WEEK: 200528 <200528/EW>  
 FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s WNT

1265 WNT  
 148 WNTS  
 L29 1307 WNT  
 (WNT OR WNTS)

=> s l29 (s) antag?

48582 ANTAG?  
 L30 161 L29 (S) ANTAG?

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106 DICKKOPF  
 4 DICKKOPFS  
 107 DICKKOPF  
 (DICKKOPF OR DICKKOPFS)  
 920163 1  
 20 DICKKOPF (W) 1  
 178 DKK  
 16 DKKS  
 181 DKK  
 (DKK OR DKKS)  
 920163 1  
 40 DKK (W) 1  
 L31 46 (DICKKOPF (W) 1) OR (DKK (W) 1)

=> s dickkopf-1 or DKK1 or DKK-1

106 DICKKOPF  
 4 DICKKOPFS

107 DICKKOPF  
 (DICKKOPF OR DICKKOPFS)  
 920163 1  
 20 DICKKOPF-1  
 (DICKKOPF(W)1)  
 26 DKK1  
 178 DKK  
 16 DKKS  
 181 DKK  
 (DKK OR DKKS)  
 920163 1  
 40 DKK-1  
 (DKK(W)1)  
 L32 62 DICKKOPF-1 OR DKK1 OR DKK-1

=> s l32 or l31  
 L33 62 L32 OR L31

=> s osteo?  
 L34 27031 OSTEO?

=> s l34 or bone  
 48366 BONE  
 8795 BONES  
 50481 BONE  
 (BONE OR BONES)  
 L35 59451 L34 OR BONE

=> s cancer? or tumor? or neoplas?  
 70033 CANCER?  
 58772 TUMOR?  
 20120 NEOPLAS?  
 L36 87552 CANCER? OR TUMOR? OR NEOPLAS?

=> s myeloma  
 14084 MYELOMA  
 1344 MYELOMAS  
 L37 14570 MYELOMA  
 (MYELOMA OR MYELOMAS)

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
 L2 244 S L1 (S) ANTAGON?  
 L3 553450 S OSTEO? OR BONE  
 L4 70 S L3 AND L2  
 L5 22597 S MULTIPLE MYELOMA  
 L6 1 S L5 AND L4  
 L7 1 S L2 AND L5  
 L8 31029 S MYELOMA  
 L9 1 S L8 AND L2  
 L10 451 S L1 AND L3  
 L11 7 S L10 AND L5  
 L12 1 S L11 NOT PY>2002  
 L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
 L14 2 S L13 AND L11  
 L15 19 S L13 AND L3  
 L16 14 S L15 AND EXPRESS?  
 L17 6 S L16 NOT PY>2002

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005

L18 4365 S WNT

L19 273 S L1 (S) ANTAGON?  
 L20 273 S L18 (S) ANTAGON?  
 L21 16913 S MYELOMA  
 L22 5 S L20 AND L21  
 L23 123 S (DICKKOPF () 1) OR (DKK () 1)  
 L24 155 S DICKKOPF-1 OR DKK1  
 L25 170 S L23 OR L24  
 L26 61795 S OSTEO?  
 L27 32 S L26 AND L25  
 L28 7 S L27 AND L21

FILE 'PCTFULL' ENTERED AT 13:10:21 ON 25 JUL 2005

L29 1307 S WNT  
 L30 161 S L29 (S) ANTAG?  
 L31 46 S (DICKKOPF () 1) OR (DKK () 1)  
 L32 62 S DICKKOPF-1 OR DKK1 OR DKK-1  
 L33 62 S L32 OR L31  
 L34 27031 S OSTEO?  
 L35 59451 S L34 OR BONE  
 L36 87552 S CANCER? OR TUMOR? OR NEOPLAS?  
 L37 14570 S MYELOMA

=> s 162 and 135

L62 NOT FOUND.

The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s 133 and 134

L38 39 L33 AND L34

=> s 138 and 137

L39 18 L38 AND L37

=> s 139 not py>2002

287458 PY>2002

L40 8 L39 NOT PY>2002

=> s 133/clm

16 DICKKOPF/CLM  
 870322 1/CLM  
 3 DICKKOPF-1/CLM  
 ((DICKKOPF(W)1)/CLM)  
 5 DKK1/CLM  
 26 DKK/CLM  
 870322 1/CLM  
 5 DKK-1/CLM  
 ((DKK(W)1)/CLM)  
 16 DICKKOPF/CLM  
 870322 1/CLM  
 3 DICKKOPF/CLM (W) 1/CLM  
 26 DKK/CLM  
 870322 1/CLM  
 5 DKK/CLM (W) 1/CLM

L41 10 ((DICKKOPF-1/CLM OR DKK1/CLM OR DKK-1/CLM) OR ((DICKKOPF/CLM  
 (W) 1/CLM) OR (DKK/CLM (W) 1/CLM)))

=> s 141 and 140

L42 1 L41 AND L40

=> d ibib

L42 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ACCESSION NUMBER: 2002066509 PCTFULL ED 20020910 EW 200235  
 TITLE (ENGLISH): TREATMENT INVOLVING DKK-1 OR  
 ANTAGONISTS THEREOF

TITLE (FRENCH): TRAITEMENT FAISANT APPEL A DKK-1 OU  
 AUX ANTAGONISTES DE DKK-1  
 INVENTOR(S): DeALMEIDA, Venita I., 3014 Los Prados Avenue, #A116,  
 San Mateo, CA 94403, US;  
 STEWART, Timothy A., 465 Douglas Street, San Francisco,  
 CA 94114, US  
 PATENT ASSIGNEE(S): GENENTECH, INC., 1 DNA Way, South San Francisco, CA  
 94080, US [US, US]  
 AGENT: HASAK, Janet E.\$, GENENTECH, INC., MS 49, 1 DNA Way,  
 South San Francisco, CA 94080-4990\$, US  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002066509	A2	20020829

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID  
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
 MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI  
 SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW  
 RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
 RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
 RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 TR  
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG  
 APPLICATION INFO.: WO 2002-US4573 A 20020215  
 PRIORITY INFO.: US 2001-60/269,435 20010216

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(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
 L2 244 S L1 (S) ANTAGON?  
 L3 553450 S OSTEO? OR BONE  
 L4 70 S L3 AND L2  
 L5 22597 S MULTIPLE MYELOMA  
 L6 1 S L5 AND L4  
 L7 1 S L2 AND L5  
 L8 31029 S MYELOMA  
 L9 1 S L8 AND L2  
 L10 451 S L1 AND L3  
 L11 7 S L10 AND L5  
 L12 1 S L11 NOT PY>2002  
 L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
 L14 2 S L13 AND L11  
 L15 19 S L13 AND L3  
 L16 14 S L15 AND EXPRESS?  
 L17 6 S L16 NOT PY>2002

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005

L18 4365 S WNT  
 L19 273 S L1 (S) ANTAGON?  
 L20 273 S L18 (S) ANTAGON?  
 L21 16913 S MYELOMA  
 L22 5 S L20 AND L21  
 L23 123 S (DICKKOPF () 1) OR (DKK () 1)  
 L24 155 S DICKKOPF-1 OR DKK1  
 L25 170 S L23 OR L24  
 L26 61795 S OSTEO?

L27 32 S L26 AND L25  
L28 7 S L27 AND L21

FILE 'PCTFULL' ENTERED AT 13:10:21 ON 25 JUL 2005

L29 1307 S WNT  
L30 161 S L29 (S) ANTAG?  
L31 46 S (DICKKOPF () 1) OR (DKK () 1)  
L32 62 S DICKKOPF-1 OR DKK1 OR DKK-1  
L33 62 S L32 OR L31  
L34 27031 S OSTEO?  
L35 59451 S L34 OR BONE  
L36 87552 S CANCER? OR TUMOR? OR NEOPLAS?  
L37 14570 S MYELOMA  
L38 39 S L33 AND L34  
L39 18 S L38 AND L37  
L40 8 S L39 NOT PY>2002  
L41 10 S L33/CLM  
L42 1 S L41 AND L40

=> s 133/ab

5 DICKKOPF/AB  
221598 1/AB  
3 DICKKOPF-1/AB  
((DICKKOPF(W)1)/AB)  
1 DKK1/AB  
5 DKK/AB  
221598 1/AB  
2 DKK-1/AB  
((DKK(W)1)/AB)  
5 DICKKOPF/AB  
221598 1/AB  
3 DICKKOPF/AB (W) 1/AB  
5 DKK/AB  
221598 1/AB  
2 DKK/AB (W) 1/AB  
L43 4 ((DICKKOPF-1/AB OR DKK1/AB OR DKK-1/AB) OR ((DICKKOPF/AB (W)  
1/AB) OR (DKK/AB (W) 1/AB)))

=> s 142 and 135

L44 1 L42 AND L35

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L44 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN  
 TIEN TREATMENT INVOLVING DKK-1 OR ANTAGONISTS THEREOF  
 TIFR TRAITEMENT FAISANT APPEL A DKK-1 OU AUX ANTAGONISTES  
 DE DKK-1  
 ABEN Antagonists to Dickkopf-1 (Dkk-1  
 ) proteins are administered in effective amounts to treat disorders  
 involving insulin resistance, such as non-insulin-dependent diabetes  
 mellitus (NIDDM), hypoinsulinemia, and disorders involving muscle  
 atrophy, trauma, or degeneration. Preferably, the antagonists are  
 composed of compositions comprising antibodies directed to Dkk  
 -1 in a pharmaceutically acceptable carrier for use in  
 blocking the effects of Dkk-1. Additionally provided  
 is a method of treating obesity or hyperinsulinemia in a mammal by  
 administering an effective amount of Dkk-1 to a  
 mammal. Also provided are methods of diagnosing insulin resistance,  
 hyper- and hypoinsulinemia, obesity, and related disorders using  
 Dkk-1 as a target and non-human transgenic animals  
 that overexpress <i>dkk-1</i> nucleic acid.  
 ABFR L'invention concerne un traitement consistant a administrer des  
 antagonistes des proteines Dickkopf-1 (Dkk  
 -1) en quantites efficaces pour traiter les troubles  
 impliquant une resistance insulinerie, tels que le diabete non  
 insulino-dependant (NIDDM), l'hypoinsulinemie et les troubles impliquant  
 une atrophie musculaire, un traumatisme ou une degeneration. Ces  
 antagonistes sont avantageusement composes d'anticorps diriges contre  
 Dkk-1 dans un excipient pharmaceutiquement acceptable  
 et utilises pour bloquer les effets de Dkk-1.  
 L'invention concerne egalement une methode de traitement de l'obesite ou  
 de l'hyperinsulinemie chez un mammifere, consistant a administrer une  
 quantite efficace de Dkk-1 a un patient. L'invention  
 concerne egalement des methodes permettant de diagnostiquer la  
 resistance insulinerie, l'hyper- et l'hypoinsulinemie, l'obesite et les  
 troubles associes, a l'aide de Dkk-1 comme cible et  
 des animaux transgeniques non humains surexprimant l'acide nucleique <i>  
 dkk-1</i>.  
 DETD TREATMENT INVOLVING DKK-1 OR ANTAGONISTS THEREOF  
 Background of the Invention  
 Field of the Invention  
 The present invention provides for the diagnosis and treatment of  
 disorders involving. . . hyperinsulinemia and for repairing and  
 regenerating muscle in  
 mammals. More particularly, the present invention relates to the use of  
 Dickkopf- I (Dkk- 1) protein to treat  
 obesity and hyperinsulinemia and to the use of antagonists that bind to  
 Dkk- I and/or neutralize its activity. . .  
 Dkk-I (WO 99/46281 published Sept. 16, 1999, wherein the Dkk-  
 1 is designated as PRO1008 and is

encoded by DNA57530; WO 00/18914 published April 6, 2000; WO 00/52047 published September 8, 2000; WO. . .

as polycystic ovarian disease, dermatological disorders such as infections, varicose veins, Acanthosis nigricans, and eczema, exercise intolerance, insulin resistance, hypertension, hypercholesterolemia, cholelithiasis, osteoarthritis, orthopedic injury, thromboembolic disease, cancer, and coronary heart disease. Rissanen et al., British Medical Journal, 301.

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#### Summary of the Invention

Accordingly, antagonists to Dkk-1, such as antibodies, are herein disclosed to be useful in the treatment of insulin resistance associated with, for example, glucose intolerance,. . .

mammal in need thereof an effective amount of an antagonist to Dkk Preferably, the mammal is human, the Dkk-I is human Dkk-1, and/or the human has NIDDM. Also preferred is systemic administration. The antagonist is preferably, an antibody that binds Dkk- 1, and more preferably a monoclonal antibody that binds Dkk- 1, and still more preferably one that neutralizes an insulin-resistance or hypoinsulinemic activity of Dkk Most preferred is a monoclonal antibody prepared from. . .

Preferably, the measuring is carried out using an anti-Dkk-1 antibody, such as a monoclonal antibody, in an immunoassay, Also, preferably such anti-Dkk-1 antibody comprises a label, more preferably a fluorescent label, a radioactive label, or an enzyme label, such as a bioluminescent label. . .

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Additionally provided is a monoclonal antibody preparation prepared by hyperimmunizing mice with tagged Dkk- 1 (preferably purified recombinant polyhistidine-tagged human Dkk-I) diluted in an adjuvant, fusing B-cells from the mice having anti-Dkk-1 antibody titers (preferably high titers) with mouse myeloma cells and obtaining supernatants, harvesting the supernatants, screening the harvested supernatants for antibody production,. . .

a candidate pharmaceutical drug on insulin resistance, hypoinsulinemia, or muscle repair comprising administering said drug to a non-human transgenic animal that overexpresses dkk-1 nucleic acid and determining the effect of the drug on glucose clearance from the blood of said animal, on circulating insulin. . . the animal is a rodent, more preferably a mouse or rat, and most preferably a mouse. In another preferred embodiment, the dkk-1 nucleic acid overexpressed by the animal is under the control of a muscle-specific promoter, and the cDNA is overexpressed in muscle. . .

- (a) a container comprising an antibody that binds Dkk-1;
- (b) a container comprising a standard sample containing Dkk-1; and
- (c) instructions for using the antibody and standard sample to detect

insulin resistance, hypoinsulinemia, hyperinsulinemia, or obesity, wherein either the antibody. . . is detectably labeled or the kit further comprises another container comprising a second antibody that is detectably labeled and binds to the

Dkk-1 or to the antibody that binds Dkk Preferably the anti-Dkk-1 antibody of the kit is a monoclonal antibody, more preferably one that neutralizes an insulin-resistance, hyperinsulinemic, hypoinsulinemic, or obesity activity of Dkk-1.

for detecting the presence or onset of obesity or hyperinsulinemia in a mammal comprising the steps of-  
(a) measuring the amount of Dkk-1 in a sample from said mammal; and  
(b) comparing the amount determined in step (a) to an amount of Dkk-1 present in a standard sample, a decreased level in the amount of Dkk-1 in step (a) being indicative of obesity or hyperinsulinemia.

Preferably, the measuring is carried out using an anti-Dkk-1 antibody in an immunoassay. Also, preferably the anti-Dkk-1 antibody comprises a label. The preferred labels and immunoassays are those as

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set. . .

In a preferred embodiment the Dkk-1 is human Dkk-1 in the kit and it may further comprise a container with a weight-loss agent.

effect of a candidate pharmaceutical drug on obesity or hyperinsulinemia comprising administering said drug, to a non-human binary transgenic animal that expresses dkk-1 nucleic acid and determining the effect of the drug on an obesity-determining property or on the level of insulin in said. . .

The invention also provides a non-human transgenic animal that overexpresses dkk-1 nucleic acid.

method for repairing or regenerating muscle in a mammal comprising administering to the mammal an effective amount of an antagonist to Dkk-1, preferably an antibody that binds to Dkk Preferably, the mammal is human and/or the antibody is a monoclonal antibody.

(a) a container comprising an antagonist to Dkk-1, preferably an antibody that binds Dkk-1; and  
(b) instructions for using the antagonist to repair or regenerate muscle in a mammal.

Figure 2 shows a gel of human Dkk-1 expressed in baculovirus and its clipping.

Figure 3A shows the effects of human Dkk-1 (dark bars) on basal glucose uptake in L6 muscle cells for 2, 6, and 26 hours. Figures 3B and 3C show, respectively, the effects of human Dkk-1 on basal (light bars) and 30 nM-insulin-stimulated (dark bars) glucose uptake in L6 muscle cells.

shows the effects of human Dkk-1 on basal and insulin-dependent glucose uptake (expressed as percent control) as a function of human Dkk-1 concentration



(nM) upon 48-hour treatment.

Figure 5A-5I show respectively the effect of human Dkk-1 on the incorporation of glucose into glycogen in L6 muscle cells with (dark bars) and without (light bars) insulin for 48. . . .

Figures 8A-8D show the effect of 40 nM human Dkk-1 (dark bars) on the kinase activities of PDK-I (Fig. 8A), GSK3 P (Fig. 8I3), S6 kinase (Fig. 8C), and Akt (Fig. . . . .

Figures 9A and 9B show the effect of human Dkk-1 on levels of basal (light bars) and 30 nM-insulin-stimulated (dark bars) glucose uptake of 3T3 LI cells (adipocytes) after 48-hour. . . .

Dkk-I (triangles). Figure I IB shows the insulin levels in the female FVB mice intravenously injected with saline (control), 0.05 mg/kg/day human Dkk-1, and 0.2 mg/kg/day human Dkk-1. Figure 12A shows the effects of human Dkk-1 on expression of various markers of muscle differentiation in mice injected therewith, with control (light bars) and 0.2 mg/kg/day of human. . . .

Figure 17 shows the effect of an anti-human Dkk-1 monoclonal antibody on the Dkk-1-mediated decrease in glucose uptake in L6 cells in the absence and presence of insulin, where the. . . . the L6 cells with 40 nM Dkk-I are black bars, and the L6 cells with 40 nM Dkk-I and 0.5  $\mu$ g/mL anti-Dkk-1 antibody are dark gray bars on the far right.

An insulin-resistance-treating agent is an agent other than an antagonist to Dkk-1 that is used to treat insulin resistance, such as, for example, hypoglycemic agents. Examples of such treating agents include insulin (one or. . . .

As used herein, Dkk- I or Dickkopf- 1 refers to Wnt inhibitor with properties and characteristics described in WO 99/46281 published September 16, 1999 and Glinka et al, Nature,. . . .

The expressions, antagonist, antagonist to Dkk-1, and the like within the scope of the present invention are meant to include any molecule that interacts with Dkk-1 and interferes with its function or blocks or neutralizes a relevant activity of Dkk- 1, by whatever means, depending on the indication being treated. It may prevent the interaction between Dkk-1 and one or more of its receptors. Such agents accomplish this effect in various ways. For instance, the class of antagonists that neutralize a Dkk-1 activity will bind to Dkk- I with sufficient affinity and specificity to interfere with Dkk- I as defined below.

An antibody that binds Dkk- 1 is one capable of binding to that antigen with sufficient affinity such that the antibody is useful as a therapeutic agent. . . . the Dkk-1 Included within this group of antagonists are, for example, antibodies directed against Dkk- I or portions thereof reactive with Dkk-1, the Dkk- I receptor or portions thereof reactive with Dkk-I, or any other ligand that binds to Dkk- I. The term also. . . .

neutralize the activity of are used herein to mean, for example, block, prevent, reduce, counteract the activity of, or make the Dkk-1 ineffective by any mechanism. Therefore, the antagonist may prevent a binding event necessary for activation of Dkk. By neutralizing antibody is meant an antibody molecule as herein defined that is able to block or significantly reduce an effector function of the Dkk-1. For example, a neutralizing antibody may inhibit or reduce the ability of Dkk-1 to interact with a Dkk-1 receptor. Alternatively, the neutralizing antibody may inhibit or reduce the ability of Dkk-1 to block the Dkk-1 receptor signalling pathway. The neutralizing antibody may also immunospecifically bind to the Dkk-1 in an immunoassay for Dkk-1 activity such as the ones described herein. It is a characteristic of the neutralizing antibody of.

The term non-human transgenic animal that overexpresses dkk-1 nucleic acid herein refers to a non-human animal, such as a rodent, that has included within a plurality of its cells.

The term non-human binary transgenic animal that expresses dkk-1 nucleic acid herein refers to a non-human animal, such as a rodent, in which gene expression is controlled by the interaction of Dkk-1 on a target transgene. These interactions are controlled by crossing animal lines (such as rodent, e.g., mouse lines) or by adding or.

diagnosing and treating insulin resistance and hypoinsulinemia based on antagonists that bind to, and preferably neutralize, the activity of Dkk. Further, Dkk-1 itself is a useful treatment for obesity and hyperinsulinemia.

Additionally, antagonists to Dkk-1 are further indicated in methods herein for muscle repair and regeneration.

will specifically bind to the protein used for immunization. Alternatively, lymphocytes may be immunized in vitro. Lymphocytes then are fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, pp.

in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin,

Preferred myeloma cells are those that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive to.

Among these, preferred myeloma cell lines are murine

myeloma lines, such as those derived from MOPC-21 and MPC- I I mouse tumors available from the Salk Institute Cell Distribution Center, . . .

which are then transfected into host cells such as E. coli cells, simian COS cells, Chinese Hamster Ovary (CHO) cells, or myeloma cells that do not otherwise produce antibody protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. Review articles. . .

Amino acid sequence modification(s) of the anti-Dkk-1 antibodies described herein are contemplated. For example, it may be desirable to improve the binding affinity and/or other biological properties of the. . . Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of, residues within the amino acid sequences of the anti-Dkk-1 antibody. Any combination of deletion, insertion, and substitution is made to arrive at the final construct, provided that the final construct possesses. . .

or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an anti-Dkk-1 antibody with an N-terminal methionyl residue or the antibody fused to a hypoglycemic polypeptide. Other insertional variants of the anti-Dkk- I antibody. . .

preparation by oligonucleotide-mediated (or site-directed) mutagenesis, PCR mutagenesis, or cassette mutagenesis of an earlier prepared variant or a non-variant version of the anti-Dkk- 1 antibody.

serum half-life of the therapeutic antagonist. For example, a soluble immunoglobulin chimera, such as described herein, can be obtained for each specific Dkk-1 antagonist or antagonistic portion thereof, as described in U.S. Pat. No. . .

The preferred dose is about 0.50 mg/kg/day, more preferably about 0.1 to 25 mg/kg/day. More preferred still, when the Dkk- 1 antagonist is administered daily, the intravenous or intramuscular dose for a human is about 0.3 to 10 mg/kg of body weight. . .

Preferred continuous dosing schedules include daily continuous infusion, where Dkk- I antagonist is infused each day, and continuous bolus administration schedules, where Dkk-1 antagonist is administered at least once per day by bolus injection or inhalant or intranasal routes. The invention also encompasses discontinuous. . .

will vary according to the formulation, method of delivery, and clinical needs of the mammal being treated. For example, if the Dkk- 1 antagonist is administered by infusion, administration schedules may comprise a first period of administration followed by a second period in which Dkk-. . .

the administration is by bolus injection, especially bolus injection of a slow-release

formulation, dosing schedules may also be continuous in that Dkk-1 antagonist is administered each day, or may be discontinuous, with first and second periods as described above.

dosing schedule, and route of administration for the treatment of the insulin-resistant or hypoinsulinemic disorder or muscle condition. The containers of Dkk-1 antagonist may be unit doses, bulk packages (e.g., multi-dose packages), or sub-unit doses.

resilient stopper. Ampoules with non-resilient, removable closures (e.g., sealed glass) or resilient stoppers are most conveniently used for injectable forms of Dkk-1 antagonist. Also contemplated are packages for use in combination with a specific device, such as an inhaler, a nasal administration device.

One specifically preferred method for administration of Dkk-1 is by subcutaneous infusion, particularly using a metered infusion device, such as a pump. Such pump can be reusable or disposable.

Therapeutic formulations of Dkk-1 suitable for storage include mixtures of the Dkk-1 having the desired degree of purity with pharmaceutically acceptable carriers, excipients, or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), are described in WO 97/04801. These compositions comprise Dkk-1 containing from about 0.1 to 90% by weight of the active Dkk-1, preferably in a soluble form, and more generally from about 10 to 30%.

methods. In addition, sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the Dkk-1, which matrices are in the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example,

The Dkk-1 can be joined to a carrier protein or PEG or POG or other molecule of this nature to increase its serum half-life.

For treatment of hyperinsulinemia, the administration of Dkk-1 may occur in conjunction with, for example, diazoxide (see, for example, Shaer, Nephron, 89: 337-339 (2001)).

For treatment of obesity, the administration of Dkk-1 may occur without, or may be imposed with, a dietary restriction such as a limit in daily food or calorie intake, as is desired for the individual patient. In addition, the Dkk-1 is appropriately administered in combination with other treatments for combatting or preventing obesity, known herein as weight-loss agents. Substances useful for.

These weight-loss adjunctive agents and diazoxide may be administered at the same time as, before, or after the administration of the Dkk-1 and can be administered by the same or a different administration route than the Dkk-1 is administered.

The dosages of Dkk-1 administered to an obese or hyperinsulinemic mammal will be determined by the physician in the light of the relevant circumstances, including the condition of the mammal, the type of

Dkk-1, and the chosen route of administration. The dosage is preferably at a sufficiently low level as not to cause insulin-resistance, and. . . The preferred dose is about 0.5 to 32 mg/kg/day, more preferably about 0.1 to 25 mg/kg/day. More preferred still, when the Dkk-1 is administered daily, the intravenous or intramuscular dose for a human is about 0.3 to 10 mcg/kg of body weight per. . .

Dkk-1 is administered by infusion, administration schedules may comprise a first period of administration followed by a second period in which Dkk-1 is not administered that is greater than, equal to, or less than the first period.

also provides kits for the treatment of obesity or hyperinsulinemia. The kits of the invention comprise one or more containers of Dkk-1, preferably human Dkk-1, in combination with a set of instructions, generally written instructions, relating to the use and dosage of Dkk-1 for the. . .

Dkk-1 may be packaged in any convenient, appropriate packaging. For example, if the Dkk-1 is a freeze-dried formulation, an ampoule with a resilient stopper is normally used, so that the drug may be easily reconstituted by. . .

In one embodiment, one or more of the anti-Dkk-1 antibodies used in the assay is labeled; in another embodiment, a first is unlabeled, and a labeled, second antibody is used. . .

I antibody need not be labeled, and the presence thereof can be detected using a labeled antibody which binds to the Dkk-1 antibody.

In the assays of the present invention, an antigen such as Dkk-1, or an antibody is preferably bound to a solid phase support or carrier. By solid phase support or carrier is intended. . .

a solid phase matrix, preferably a microplate. The sample is brought in contact with the Ab I-coated matrix such that any Dkk-1 in the sample to which AM is specific binds to the solid-phase AbI. Unbound sample components are removed by washing. An. . .

the diagnostic assay. For instance, such a kit can comprise an antibody or antibodies, preferably a pair of antibodies to the Dkk-1 antigen that preferably do not compete for the same binding site on the antigen. In a specific embodiment, Dkk-1 may be pre-adsorbed to the solid phase matrix. The kit preferably contains the other necessary washing reagents well-known in the art. . . the art, and some are exemplified below. The kit can optionally also comprise a Dkk-1 standard; i.e., an amount of purified Dkk-1 corresponding to a normal amount of Dkk-1 in a standard sample.

In one aspect, a kit comprises in more than one container: an antibody that binds Dkk-1, which can be coated on a solid-phase carrier, e.g., a microtiter plate, a standard sample containing Dkk-1, and instructions for use in detection, wherein the antibody that binds Dkk-1 is detectably labeled or the kit further comprises an. . .

cDNA such as murine cDNA encoding Dkk-1 or an appropriate sequence thereof can be used to clone genomic DNA encoding Dkk-1 in accordance with established techniques, and the genomic sequences are used to generate transgenic animals that contain cells that express DNA encoding Dkk-1.

transgene incorporation with tissue-specific enhancers, which results in targeted overexpression of Dkk Transgenic animals that include a copy of a transgene encoding

Dkk-1 introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased. . .

a probe that is complementary to at least a portion of the transgene. Western blot analysis

using an antibody against the Dkk-1 encoded by the transgene may be employed as an alternative or additional method for screening for the presence of the transgene. . .

specific type of cell. The most preferred such control element herein is a muscle-specific promoter that enables overexpression of the dkk-1 nucleic acid (e.g., cDNA) in muscle tissue. An example of such promoter is that described in Example I below or that. . .

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In another facet, non-human binary transgenic animals having altered dkk-1 nucleic acid expression can be used to screen candidate drugs as set forth above, such as for their ability to reduce. . .

#### Example 1

Effects of Dkk-1 *in vivo* and *in vitro*

#### Materials and Methods

##### L6 Cell culture

L6 myoblasts were proliferated in growth medium, composed of MEM alpha (Gibco-BRL). . . differentiation medium at confluence (MEM alpha with 2% fetal calf serum). Cells were grown in this medium for 3-9 days and for

Dkk-1 treatments longer than 28 hours, dkk-1 (Krupnik et al., supra; WO 99/46281; DNA encoding PRO1008) was added to this medium. Treatments. . .

#### Expression of Recombinant Dkk-1

The human homolog of Dkk-1 (hDkk-1) was expressed as a C-terminal 8X His tag fusion (see Krupnik et al., supra; and WO 99/46281, where PRO1008 is Dkk-1) in baculovirus and purified by nickel affinity column chromatography. The identity of purified protein was verified by N-terminal sequence analysis. The purified. . .

#### Glycogen Synthesis

Glycogen synthesis was determined as [ <sup>14</sup>C]glucose incorporation into

glycoeren. Control L6 cells and cells treated with dkk-1 were incubated for 2 hours in serum-free MEM alpha containing [U-14 Q glucose (5 mM crluose; 1.25 pCi/n-d) with or without. . .

Chem., 253: 7570-7578 (1978)). Differentiated cells were treated with Dkk-I at 72 hours after the induction of differentiation. For effect of Dkk-1 on 3T3L1 cell differentiation, Dkk-I was added to the medium at a concentration of 40 nM during the initiation of differentiation. . .

3' to the pRK splice donor/acceptor site that was preceded by the myosin light-chain promoter (Shani, Nature, 314: 283-286 (1985)). The dkk-1 cDNA was followed by the splice donor/acceptor sites present between the fourth and fifth exons of the human growth hormone gene (Stewart. . .

When expressed in baculovirus, the human Dkk-1 protein was clipped internally to give a 16-kDa cleavage product. In the gel shown in Fig. 2, band (a) corresponds to. . .

The Dkk-1 effects of glucose uptake are independent of the differentiation state of the cells and can be seen even in cells that. . . uptake are dose-dependent. Fig. 4B shows that the decrease in basal and insulin-dependent glucose uptake is seen upon 48-hour treatment with Dkk-1 at concentrations as low as 10 nM.

regulated the expression of genes in the insulin signaling pathway in L6 muscle cells. In particular, as shown in Fig. 7, Dkk-1 treatment increased the expression of the p85 subunit of phosphoinositide 3-kinase significantly (8.3 fold) following 48-hour treatment, but did not significantly affect. . .

Dkk- I in mice resulted in impaired glucose tolerance and reduced insulin production. Specifically, to confirm the in vivo effects of Dkk-1 seen in transgenic mice, female FVB mice were injected intravenously with Dkk-1 for 8 days (single daily injection of 0.05 and 0.2 mg/kg/day). The effects of Dkk- 1 on glucose tolerance were measured 48 hours and 8 days after the start of injection. Glucose tolerance was unaffected with 48. . .

Overexpression of Dkk-1 in mice affected growth, body composition, and metabolism. Particularly, Transcronic FVB mice overexpressing the dkk-1 transgene under control of the MLC promoter were generated (Shani, supra). Body weights of control and transgenic animals were followed over. . .

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Table 2

Control Control Dkk-I Dkk-1

Regular diet Regular diet transgenic transgenic

Physiological Parameter (males, n=8) (females, n=4) Regular diet Regular diet

males, n=4) (females, n=8)

Body Weight at 16. . .

signaling inhibits adipogenesis. To determine whether Dkk-I affected body composition, some animals were placed on a high-fat diet for 24 weeks. Dkk-

1 transgenic animals on a high-fat diet also showed significantly reduced body weights than their wild-type littermates (Fig. 15A), with comparable reduction. . .

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Table 3

Control Control Dkk-1 TG Dkk-1

TG

High-fat diet High-fat diet High-fat diet High-fat diet

eter (m=12) (f=8) m=6) (f=5)

Body Weight at 16 of

40.3  $\pm$  6.6 34.7  $\pm$  6.6 . . .

diabetes, can be affected by expression levels, phosphorylation, and activity of

proteins in the insulin- signaling pathway. Therefore, the effects of Dkk-1 in muscle both in vivo and in vitro were investigated.

animals also had reduced levels of serum insulin, although no effects were seen in the serum insulin levels in transgenic mice. Dkk-1 reduced the basal and insulin-stimulated glucose uptake in L6 cells through inhibition of Akt, a key intermediate in the insulin-signaling pathway.

These effects of Dkk-1 were seen only after 18 hrs of exposure to Dkk-1.

size with a proportional decrease in the weight of various organs. Without being limited to any one theory, these effects of Dkk-1 are likely to be mediated through the reduction in insulin (and likely IGF-1)-stimulated Akt activity. Direct evidence for this comes from studies. . .

Chem., 276: 19664-19671 (2001)). Alternatively, without limitation to any one theory, the reduced growth rate in dkk-1 transgenic animals could be a secondary effect of the reduced glucose uptake and consequent alteration in nutrient availability and metabolic rate. . .

Primary 3T3LI preadipocytes were stimulated to differentiate in the presence or absence of Dkk-1, cells were collected at different days after the start of differentiation, and the transcripts analysed for expression levels of markers of adipocyte differentiation such as AP2, PPAR $\gamma$ , CEBP $\alpha$ , and FAS. Dkk-1 treatment did not alter levels of FAS and AP2; however, PPAR $\gamma$  levels were about 2-fold reduced in Dkk-1-treated cells and C/EBP $\alpha$  levels. . .

adipose tissue mass and are up-regulated by Akt (Barthel et al., Endocrinology 138: 3559 (1997)). The reduced levels of circulating leptin in dkk-1

138: 3559

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transgenic animals could be a direct effect of decreased adipose mass and/or decreased Akt activity in adipose tissue, without being limited. . .

A significant reduction in the levels of secreted insulin was observed herein following 8 days of

Dkk-1 injection, and smaller effects in transgenic animals overexpressing dkk-1 in the muscle. Without being



limited to any one theory, the stronger effects in injected animals could be a result of. . . there may be smaller differences in insulin levels either due to compensatory mechanisms or due to a more localized effect of Dkk-1 in the muscle. Since Akt is known to stimulate islet cell proliferation and insulin production, and since the data herein show for the first time that Dkk-1-injected and transgenic mice have lower insulin levels, an antagonist to Dkk- 1 is now found useful in treating hypoinsulinemia, and conversely, Dkk- I itself is found useful in treating hyperinsulinemia.

in L6 muscle cells as well as in transgenic mice overexpressin cr the protein in muscle. Treatment of muscle cells with Dkk- 1 resulted in a decrease in the basal and insulin-stimulated glucose uptake. This effect was observed following both short-term and long-term treatment,

49

suggesting, without being limited to any one theory, that Dkk- 1 may affect both the activity as well as the expression levels of proteins in the insulin signaling pathway. Consistent with this. . .

obesity and hyperinsulinernia, as well as being useful as a diagnostic marker in assays for such conditions. Also, an antagonist to Dkk-1 is expected to inhibit the progression of the diabetes phenotype in transgenic animal models disclosed in U.S. Pat. No. 6,187,991.

#### Example 2

##### Development of Anti-Dkk-1 Monoclonal Antibodies

Five female Balb/c mice (Charles River Laboratories, Wilmington, DE) were hyperimmunized with purified recombinant polyhistidine-tagged (HIS8) human Dkk- I expressed. . . used for each animal, administered via footpad. After five injections, B-cells from the lymph nodes of the five mice, demonstrating high anti-Dkk- 1 antibody titers, were fused with mouse myeloma cells (X63.Ag8.653; American Type Culture Collection, Manassas, VA) using the protocols described in Kohler and Milstein, supra, and Hongo et al.,. . .

All the seven antibody preparations bound Dkk-1 in Western immunoblots.

L6 cells were differentiated and treated for 48 hours in the absence of Dkk-1 (control) or in the presence of 40 nM Dkk-1 (plus or minus anti-Dkk-1 antibody 1G1.2D12.2D1 1 (ATCC No. PTA-3086) in an amount of 0.5 ttg/mL). Basal and insulin-stimulated glucose uptake in the L6 cells. . .

50

Designation ATQC Dep. No. Deposit Date

DKKI.MAB3139,8CI 1.2GI 1. IDI PTA-3084 February 21, 2001

DKK1.MAB3143.4C7.2HI0.2GI PTA-3085 February 21, 2001

DKKLMAB3142. I G1.21) 12.2131 1 PTA-3086 February 21, 2001

DKK1.MAB3141.5B12.2C5.2A5 PTA-3087 February 21, 2001

DKKLMAB313 8.7C 1 1 16.2AS PTA-3088 February 21, 2001

DKK1.MAB3140.7B2.2A6.2H4 PTA-3089 February 21, 2001

DKK1.MAB3144.5A2.2A8.1C3 PTA-3097 February 21, 2001

This deposit was made under the provisions of the Budapest Treaty on the International Recognition

of the Deposit. . . .

CLMEN. . . insulin resistance or hypoinsulinemia in mammals comprising administering to a mammal in need thereof an effective amount of an antagonist to Dickkopf- 1 (Dkk- 1).

4 The method of claim 1 wherein the antagonist is an antibody that binds Dkk- 1.

5 . The method of claim 4 wherein the antibody is a monoclonal antibody.

.  
presence or onset of insulin resistance or hypoinsulinemia in a mammal comprising the steps of:

(a) measuring the amount of Dickkopf- I (Dkk- 1) in a sample from said mammal; and

(b) comparing the amount determined in step (a) to an amount of Dkk- I.

. . .  
12 The method of claim I I wherein the anti-Dkk- 1 antibody comprises a label.

16 The method of claim IO wherein the mammal is human and human Dkk- 1 is being measured.

17 A kit for treating insulin resistance or hypoinsulinemia, said kit comprising:

(a) a container comprising an antagonist to Dkk-1;  
and

(b) instructions for using the antagonist to treat insulin resistance or hypoinsulinemia.

18 The kit of claim 17 wherein the antagonist is an antibody that binds Dkk- 1

20 The kit of claim 18 wherein the antibody binds human Dkk- 1.

26 A method of treating obesity or hyperinsulinemia in mammals comprising administering to a mammal in need thereof an effective amount of Dickkopf-I (Dkk-1 ).

.  
for detecting the presence or onset of obesity or hyperinsulinemia in a mammal comprising the steps of.

(a) measuring the amount of Dickkopf-1 (Dkk]1) in a sample from said mammal; and

(b) comparing the amount determined in step (a) to an amount of Dkk-1 present in a standard sample, a decreased level in the amount of Dkk-1 in step (a) being indicative of obesity or hyperinsulinemia.

36 A kit for treating obesity or hyperinsulinemia, said kit comprising:

(a) a container comprising Dkk- 1; and

(b) instructions for using the Dkk- I to treat obesity or hyperinsulinemia.

.  
the presence or onset of insulin resistance, hyperinsulinemia, hypoinsulinemia, or obesity, said kit comprising:

(a) a container comprising an antibody that binds Dickkopf- 1 (Dkk-1);

(b) a container comprising a standard sample containing Dkk- 1; and

(c) instructions for using the antibody and standard sample to detect insulin resistance,

hyperinsulinemia, hypoinsulinemia, or obesity, wherein either the antibody. . .

41 The kit of claim 39 wherein the Dkk-1 is human Dkk-1 and the kit is for detecting non-insulin dependent diabetes or obesity.

53

. A method for repairing or regenerating muscle in a mammal comprising.  
. . .

47 A monoclonal antibody preparation prepared by hyperimmunizing mice with tagged Dkk-1 diluted in an adjuvant, fusing B-cells from the mice having anti-Dkk-I antibody titers with mouse myeloma cells and obtaining supernatants, harvesting the supernatants, screening the harvested supernatants for antibody production, injecting positive clones showing the highest immunobinding after. . .

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

L1 3942 S WNT  
L2 244 S L1 (S) ANTAGON?  
L3 553450 S OSTEO? OR BONE  
L4 70 S L3 AND L2  
L5 22597 S MULTIPLE MYELOMA  
L6 1 S L5 AND L4  
L7 1 S L2 AND L5  
L8 31029 S MYELOMA  
L9 1 S L8 AND L2  
L10 451 S L1 AND L3  
L11 7 S L10 AND L5  
L12 1 S L11 NOT PY>2002  
L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
L14 2 S L13 AND L11  
L15 19 S L13 AND L3  
L16 14 S L15 AND EXPRESS?  
L17 6 S L16 NOT PY>2002

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005

L18 4365 S WNT  
L19 273 S L1 (S) ANTAGON?  
L20 273 S L18 (S) ANTAGON?  
L21 16913 S MYELOMA  
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L23 123 S (DICKKOPF () 1) OR (DKK () 1)  
L24 155 S DICKKOPF-1 OR DKK1  
L25 170 S L23 OR L24  
L26 61795 S OSTEO?  
L27 32 S L26 AND L25  
L28 7 S L27 AND L21

FILE 'PCTFULL' ENTERED AT 13:10:21 ON 25 JUL 2005

L29 1307 S WNT  
L30 161 S L29 (S) ANTAG?  
L31 46 S (DICKKOPF () 1) OR (DKK () 1)  
L32 62 S DICKKOPF-1 OR DKK1 OR DKK-1  
L33 62 S L32 OR L31  
L34 27031 S OSTEO?  
L35 59451 S L34 OR BONE  
L36 87552 S CANCER? OR TUMOR? OR NEOPLAS?

L37 14570 S MYELOMA  
 L38 39 S L33 AND L34  
 L39 18 S L38 AND L37  
 L40 8 S L39 NOT PY>2002  
 L41 10 S L33/CLM  
 L42 1 S L41 AND L40  
 L43 4 S L33/AB  
 L44 1 S L42 AND L35

=> s d ibib  
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 18 IBIB  
 L45 0 D IBIB  
 (D(W)IBIB)

=> d l44 ibib

L44 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ACCESSION NUMBER: 2002066509 PCTFULL ED 20020910 EW 200235  
 TITLE (ENGLISH): TREATMENT INVOLVING DKK-1 OR  
 ANTAGONISTS THEREOF  
 TITLE (FRENCH): TRAITEMENT FAISANT APPEL A DKK-1 OU  
 AUX ANTAGONISTES DE DKK-1  
 INVENTOR(S): DeALMEIDA, Venita I., 3014 Los Prados Avenue, #A116,  
 San Mateo, CA 94403, US;  
 STEWART, Timothy A., 465 Douglas Street, San Francisco,  
 CA 94114, US  
 PATENT ASSIGNEE(S): GENENTECH, INC., 1 DNA Way, South San Francisco, CA  
 94080, US [US, US]  
 AGENT: HASAK, Janet E.\$, GENENTECH, INC., MS 49, 1 DNA Way,  
 South San Francisco, CA 94080-4990\$, US  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002066509	A2	20020829

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
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 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
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 RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
 RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
 RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 TR  
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG  
 APPLICATION INFO.: WO 2002-US4573 A 20020215  
 PRIORITY INFO.: US 2001-60/269,435 20010216

=> file dissab  
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 ENTRY SESSION  
 FULL ESTIMATED COST 16.18 62.30

FILE 'DISSABS' ENTERED AT 13:16:14 ON 25 JUL 2005  
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=> s dickkopf-1 or DKK1 or DKK-1  
2 DICKKOPF  
1 DICKKOPFS  
3 DICKKOPF  
(DICKKOPF OR DICKKOPFS)  
354082 1  
2 DICKKOPF-1  
(DICKKOPF(W)1)  
2 DKK1  
3 DKK  
1 DKKS  
3 DKK  
(DKK OR DKKS)  
354082 1  
2 DKK-1  
(DKK(W)1)  
L46 4 DICKKOPF-1 OR DKK1 OR DKK-1

=> s osteo?  
L47 3245 OSTEO?

=> s l47 and l46  
L48 0 L47 AND L46

=> s l46 and myeloma  
547 MYELOMA  
32 MYELOMAS  
567 MYELOMA  
(MYELOMA OR MYELOMAS)  
L49 0 L46 AND MYELOMA

=> d his

(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

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L6 1 S L5 AND L4  
L7 1 S L2 AND L5  
L8 31029 S MYELOMA  
L9 1 S L8 AND L2  
L10 451 S L1 AND L3  
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L12 1 S L11 NOT PY>2002  
L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
L14 2 S L13 AND L11  
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L16 14 S L15 AND EXPRESS?  
L17 6 S L16 NOT PY>2002

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005

L18 4365 S WNT  
L19 273 S L1 (S) ANTAGON?  
L20 273 S L18 (S) ANTAGON?

L21 16913 S MYELOMA  
 L22 5 S L20 AND L21  
 L23 123 S (DICKKOPF () 1) OR (DKK () 1)  
 L24 155 S DICKKOPF-1 OR DKK1  
 L25 170 S L23 OR L24  
 L26 61795 S OSTEO?  
 L27 32 S L26 AND L25  
 L28 7 S L27 AND L21

FILE 'PCTFULL' ENTERED AT 13:10:21 ON 25 JUL 2005

L29 1307 S WNT  
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 L31 46 S (DICKKOPF () 1) OR (DKK () 1)  
 L32 62 S DICKKOPF-1 OR DKK1 OR DKK-1  
 L33 62 S L32 OR L31  
 L34 27031 S OSTEO?  
 L35 59451 S L34 OR BONE  
 L36 87552 S CANCER? OR TUMOR? OR NEOPLAS?  
 L37 14570 S MYELOMA  
 L38 39 S L33 AND L34  
 L39 18 S L38 AND L37  
 L40 8 S L39 NOT PY>2002  
 L41 10 S L33/CLM  
 L42 1 S L41 AND L40  
 L43 4 S L33/AB  
 L44 1 S L42 AND L35  
 L45 0 S D IBIB

FILE 'DISSABS' ENTERED AT 13:16:14 ON 25 JUL 2005

L46 4 S DICKKOPF-1 OR DKK1 OR DKK-1  
 L47 3245 S OSTEO?  
 L48 0 S L47 AND L46  
 L49 0 S L46 AND MYELOMA

=> file pctfull

COST IN U.S. DOLLARS

SINCE FILE  
ENTRY

TOTAL  
SESSION

FULL ESTIMATED COST

0.82

63.12

FILE 'PCTFULL' ENTERED AT 13:17:23 ON 25 JUL 2005

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FILE LAST UPDATED: 19 JUL 2005 <20050719/UP>  
 MOST RECENT UPDATE WEEK: 200528 <200528/EW>  
 FILE COVERS 1978 TO DATE

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=> s 143 and 135

L50 4 L43 AND L35

=> d ibib 1-4

L50 ANSWER 1 OF 4 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ACCESSION NUMBER: 2005049640 PCTFULL ED 20050607 EW 200522  
 TITLE (ENGLISH): RHESUS MONKEY DICKKOPF-1, NUCLEOTIDES ENCODING SAME,  
 AND USES THEREOF  
 TITLE (FRENCH): PROTEINE DICKKOPF-1 DE SINGE RHESUS, NUCLEOTIDES CODANT  
 LADITE PROTEINE, ET PROCEDES D'UTILISATION  
 INVENTOR(S): HARADA, Shun-ichi, 126 East Lincoln Avenue, Rahway, NJ  
 07065-0907, US [JP, US];  
 KASPARCOVA, Viera, 126 East Lincoln Avenue, Rahway, NJ  
 07065-0907, US [CZ, US];  
 GLANTSCHNIG, Helmut, 126 East Lincoln Avenue, Rahway,  
 NJ 07065-0907, US [AT, US]

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07065-0907, US [US, US], for all designates States  
except US;  
HARADA, Shun-ichi, 126 East Lincoln Avenue, Rahway, NJ  
07065-0907, US [JP, US], for US only;  
KASPARCOVA, Viera, 126 East Lincoln Avenue, Rahway, NJ  
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GLANTSCHNIG, Helmut, 126 East Lincoln Avenue, Rahway,  
NJ 07065-0907, US [AT, US], for US only  
AGENT: MERCK & CO., INC.\$, 126 East Lincoln Avenue, Rahway, NJ  
07065-0907\$, US  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005049640	A2	20050602

# DESIGNATED STATES

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AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO  
CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR  
HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV  
MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO  
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ  
VC VN YU ZA ZM ZW

RW (ARIPO):

BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

RW (EAPO):

AM AZ BY KG KZ MD RU TJ TM

RW (EPO):

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT  
LU MC NL PL PT RO SE SI SK TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2004-US38489 A 20041112

PRIORITY INFO.:

US 2003-60/520,708 20031117

L50 ANSWER 2 OF 4

ACCESSION NUMBER:

PCTFULL COPYRIGHT 2005 Univentio on STN

TITLE (ENGLISH):

2004053063 PCTFULL ED 20040630 EW 200426

TITLE (FRENCH):

MOLECULAR DETERMINANTS OF MYELOMA BONE

DISEASE AND USES THEREOF

DETERMINANTS MOLECULAIRES DE MALADIE OSSEUSE DE TYPE

MYELOME ET UTILISATIONS DE CEUX-CI

INVENTOR(S):

SHAUGHNESSY, John, D., 4317 Old Oak Drive, Little Rock,  
AR 72222, US

PATENT ASSIGNEE(S):

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2404 North University Avenue, Little Rock, AR  
72207-3608, US [US, US]

AGENT:

ADLER, Benjamin, A.\$, Adler & Associates, 8011 Candle  
Lane, Houston, TX 77071\$, US

LANGUAGE OF FILING:

English

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2004053063	A2	20040624

# DESIGNATED STATES

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AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
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KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT  
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RW (ARIPO):

BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO):

AM AZ BY KG KZ MD RU TJ TM

RW (EPO):

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
MC NL PT RO SE SI SK TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2003-US38372 A 20031204

PRIORITY INFO.:

US 2002-60/431,040 20021205

L50 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ACCESSION NUMBER: 2002092015 PCTFULL ED 20021210 EW 200247  
 TITLE (ENGLISH): REAGENTS AND METHODS FOR MODULATING DKK-MEDIATED INTERACTIONS  
 TITLE (FRENCH): REACTIFS ET PROCEDES DESTINES A MODULER DES INTERACTIONS INDUITES PAR DKK  
 INVENTOR(S): ALLEN, Kristina, 11 Oliver Lane, Hopkinton, MA 01748-3108, US [US, US];  
 ANISOWICZ, Anthony, 50 Upham Street, West Newton, MA 02465, US [US, US];  
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 DAMAGNEZ, Veronique, 125 Water Street, Framingham, MA 01701, US [FR, US];  
 ROBINSON, John, Allen, 23 Webb Road, Downingtown, PA 19335, US [US, US];  
 YAWORSKY, Paul, J., 13 Hobart Lane, Rockland, MA 02370, US [US, US]  
 PATENT ASSIGNEE(S): GENOME THERAPEUTICS CORPORATION, 100 Beaver Street, Waltham, MA 02453, US [US, US], for all designates States except US;  
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 ALLEN, Kristina, 11 Oliver Lane, Hopkinton, MA 01748-3108, US [US, US], for US only;  
 ANISOWICZ, Anthony, 50 Upham Street, West Newton, MA 02465, US [US, US], for US only;  
 BHAT, Bheem, M., 1214 Mayapple Lane, West Chester, PA 19380, US [IN, US], for US only;  
 DAMAGNEZ, Veronique, 125 Water Street, Framingham, MA 01701, US [FR, US], for US only;  
 ROBINSON, John, Allen, 23 Webb Road, Downingtown, PA 19335, US [US, US], for US only;  
 YAWORSKY, Paul, J., 13 Hobart Lane, Rockland, MA 02370, US [US, US], for US only  
 AGENT: REA, Teresa, Stanek\$, Burns, Doane, Swecker & Mathis L.L.P., P.O. Box 1404, Alexandria, VA 22313-1404\$, US  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002092015	A2	20021121

DESIGNATED STATES

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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

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RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-US15982 A 20020517

PRIORITY INFO.: US 2001-60/291,311 20010517

US 2002-60/353,058 20020201

US 2002-60/361,293 20020304

L50 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ACCESSION NUMBER: 2002066509 PCTFULL ED 20020910 EW 200235  
 TITLE (ENGLISH): TREATMENT INVOLVING DKK-1 OR ANTAGONISTS THEREOF  
 TITLE (FRENCH): TRAITEMENT FAISANT APPEL A DKK-1 OU AUX ANTAGONISTES DE



INVENTOR(S): DKK-1  
DeALMEIDA, Venita I., 3014 Los Prados Avenue, #A116,  
San Mateo, CA 94403, US;  
STEWART, Timothy A., 465 Douglas Street, San Francisco,  
CA 94114, US  
PATENT ASSIGNEE(S): GENENTECH, INC., 1 DNA Way, South San Francisco, CA  
94080, US [US, US]  
AGENT: HASAK, Janet E.\$, GENENTECH, INC., MS 49, 1 DNA Way,  
South San Francisco, CA 94080-4990\$, US  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2002066509	A2	20020829
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APPLICATION INFO.:	WO 2002-US4573	A	20020215
PRIORITY INFO.:	US 2001-60/269,435		20010216

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(FILE 'HOME' ENTERED AT 13:01:12 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 13:01:25 ON 25 JUL 2005

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L2 244 S L1 (S) ANTAGON?  
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L7 1 S L2 AND L5  
L8 31029 S MYELOMA  
L9 1 S L8 AND L2  
L10 451 S L1 AND L3  
L11 7 S L10 AND L5  
L12 1 S L11 NOT PY>2002  
L13 70 S (DICKKOPF () 1) OR (DKK () 1)  
L14 2 S L13 AND L11  
L15 19 S L13 AND L3  
L16 14 S L15 AND EXPRESS?  
L17 6 S L16 NOT PY>2002

FILE 'CAPLUS' ENTERED AT 13:06:53 ON 25 JUL 2005

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L25 170 S L23 OR L24  
L26 61795 S OSTEO?  
L27 32 S L26 AND L25

L28 7 S L27 AND L21

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L37 14570 S MYELOMA  
L38 39 S L33 AND L34  
L39 18 S L38 AND L37  
L40 8 S L39 NOT PY>2002  
L41 10 S L33/CLM  
L42 1 S L41 AND L40  
L43 4 S L33/AB  
L44 1 S L42 AND L35  
L45 0 S D IBIB

FILE 'DISSABS' ENTERED AT 13:16:14 ON 25 JUL 2005

L46 4 S DICKKOPF-1 OR DKK1 OR DKK-1  
L47 3245 S OSTEO?  
L48 0 S L47 AND L46  
L49 0 S L46 AND MYELOMA

FILE 'PCTFULL' ENTERED AT 13:17:23 ON 25 JUL 2005

L50 4 S L43 AND L35

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.34	68.46

STN INTERNATIONAL LOGOFF AT 13:18:35 ON 25 JUL 2005

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
 NEWS 2 "Ask CAS" for self-help around the clock  
 NEWS 3 FEB 28 PATDPAFULL - New display fields provide for legal status  
 data from INPADOC  
 NEWS 4 FEB 28 BABS - Current-awareness alerts (SDIs) available  
 NEWS 5 MAR 02 GBFULL: New full-text patent database on STN  
 NEWS 6 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced  
 NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
 NEWS 8 MAR 22 KOREAPAT now updated monthly; patent information enhanced  
 NEWS 9 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY  
 NEWS 10 MAR 22 PATDPASPC - New patent database available  
 NEWS 11 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags  
 NEWS 12 APR 04 EPFULL enhanced with additional patent information and new  
 fields  
 NEWS 13 APR 04 EMBASE - Database reloaded and enhanced  
 NEWS 14 APR 18 New CAS Information Use Policies available online  
 NEWS 15 APR 25 Patent searching, including current-awareness alerts (SDIs),  
 based on application date in CA/CAPLUS and USPATFULL/USPAT2  
 may be affected by a change in filing date for U.S.  
 applications.  
 NEWS 16 APR 28 Improved searching of U.S. Patent Classifications for  
 U.S. patent records in CA/CAPLUS  
 NEWS 17 MAY 23 GBFULL enhanced with patent drawing images  
 NEWS 18 MAY 23 REGISTRY has been enhanced with source information from  
 CHEMCATS  
 NEWS 19 JUN 06 The Analysis Edition of STN Express with Discover!  
 (Version 8.0 for Windows) now available  
 NEWS 20 JUN 13 RUSSIAPAT: New full-text patent database on STN  
 NEWS 21 JUN 13 FRFULL enhanced with patent drawing images  
 NEWS 22 JUN 27 MARPAT displays enhanced with expanded G-group definitions  
 and text labels  
 NEWS 23 JUL 01 MEDICONF removed from STN  
 NEWS 24 JUL 07 STN Patent Forums to be held in July 2005  
 NEWS 25 JUL 13 SCISEARCH reloaded  
 NEWS 26 JUL 20 Powerful new interactive analysis and visualization software,  
 STN AnaVist, now available  
  
 NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT  
 MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
 AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005  
  
 NEWS HOURS STN Operating Hours Plus Help Desk Availability  
 NEWS INTER General Internet Information  
 NEWS LOGIN Welcome Banner and News Items  
 NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
 NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

\*ENCOMPAT - EnCompass Patent File 1964-present (Supporters)  
 \*ENCOMPAT2 - EnCompass Patent File 1964-Present (Non-Supporters)

\* The files listed above are temporarily unavailable.

FILE 'HOME' ENTERED AT 16:15:45 ON 25 JUL 2005

=> file medline  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FILE 'MEDLINE' ENTERED AT 16:16:12 ON 25 JUL 2005

FILE LAST UPDATED: 23 JUL 2005 (20050723/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP  
RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> s bone

424243 BONE  
91740 BONES

L1 446342 BONE  
(BONE OR BONES)

=> s (dickkopf () 1) or (dickkopf-1) or dickkopf1 or (dkk1) or (dkk-1) or (dkk () 1)

85 DICKKOPF  
8 DICKKOPFS  
90 DICKKOPF  
(DICKKOPF OR DICKKOPFS)

3513889 1  
49 DICKKOPF (W) 1  
85 DICKKOPF  
8 DICKKOPFS  
90 DICKKOPF  
(DICKKOPF OR DICKKOPFS)

3513889 1  
49 DICKKOPF-1  
(DICKKOPF(W)1)  
17 DICKKOPF1  
106 DKK1  
119 DKK  
9 DKKS  
121 DKK

(DKK OR DKKS)  
3513889 1  
44 DKK-1  
(DKK(W)1)  
119 DKK  
9 DKKS  
121 DKK  
(DKK OR DKKS)

3513889 1  
44 DKK (W) 1

L2 133 (DICKKOPF (W) 1) OR (DICKKOPF-1) OR DICKKOPF1 OR (DKK1) OR (DKK-1) OR (DKK (W) 1)

=> s 12 and 11

L3 36 L2 AND L1

=> s l3 not py>2002

1489868 PY>2002

L4 12 L3 NOT PY>2002

=> s l4 and express?

932565 EXPRESS?

L5 9 L4 AND EXPRESS?

=> d ibib 1-4

L5 ANSWER 1 OF 9

MEDLINE on STN

ACCESSION NUMBER: 2002693855 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12455632

TITLE: Bmp, Fgf and Wnt signalling in programmed cell death and chondrogenesis during vertebrate limb development: the role of Dickkopf-1.

AUTHOR: Grotewold Lars; Ruther Ulrich

CORPORATE SOURCE: Institut fur Entwicklungs- und Molekularbiologie der Tiere (EMT), Heinrich-Heine-Universitat, Dusseldorf, Germany.

SOURCE: International journal of developmental biology, (2002) 46 (7) 943-7.

Journal code: 8917470. ISSN: 0214-6282.

PUB. COUNTRY: Spain

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200306

ENTRY DATE: Entered STN: 20021214

Last Updated on STN: 20030619

Entered Medline: 20030618

L5 ANSWER 2 OF 9

MEDLINE on STN

ACCESSION NUMBER: 2002131765 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11867524

TITLE: The Wnt antagonist Dickkopf-1 is regulated by Bmp signaling and c-Jun and modulates programmed cell death.

AUTHOR: Grotewold Lars; Ruther Ulrich

CORPORATE SOURCE: Entwicklungs- und Molekularbiologie der Tiere, Heinrich-Heine Universitat, D-40225 Dusseldorf, Germany.. lars.grotewold@uni-duesseldorf.de

SOURCE: EMBO journal, (2002 Mar 1) 21 (5) 966-75.

Journal code: 8208664. ISSN: 0261-4189.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200205

ENTRY DATE: Entered STN: 20020228

Last Updated on STN: 20020515

Entered Medline: 20020514

L5 ANSWER 3 OF 9

MEDLINE on STN

ACCESSION NUMBER: 2001447406 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11291860

TITLE: The role of the homeodomain protein Bozozok in zebrafish axis formation.

AUTHOR: Solnica-Krezel L; Driever W

CORPORATE SOURCE: Department of Molecular Biology, Vanderbilt University, Nashville, Tennessee 37235, USA.. lilianna.solnica-krezel@vanderbilt.edu

SOURCE: International journal of developmental biology, (2001) 45 (1) 299-310.

PUB. COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

L5 ANSWER 4 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 2001447398 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11291852  
TITLE: Dickkopfl and the Spemann-Mangold head organizer.  
AUTHOR: Niehrs C; Kazanskaya O; Wu W; Glinka A  
CORPORATE SOURCE: Division of Molecular Embryology, Deutsches  
Krebsforschungszentrum, Heidelberg, Germany.  
SOURCE: International journal of developmental biology, (2001) 45  
(1) 237-40. Ref: 34  
Journal code: 8917470. ISSN: 0214-6282.

PUB. COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

=> d ibib 5-7

L5 ANSWER 5 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 2001168646 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11269304  
TITLE: Development. The path to the heart and the road not taken.  
AUTHOR: Olson E N  
CORPORATE SOURCE: Department of Molecular Biology, University of Texas  
Southwestern Medical Center, Dallas, TX 75390, USA..  
eolson@hamon.swmed.edu  
SOURCE: Science, (2001 Mar 23) 291 (5512) 2327-8.  
Journal code: 0404511. ISSN: 0036-8075.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200104  
ENTRY DATE: Entered STN: 20010417  
Last Updated on STN: 20021218  
Entered Medline: 20010412

L5 ANSWER 6 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 2001150174 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11159911  
TITLE: Wnt antagonism initiates cardiogenesis in Xenopus laevis.  
AUTHOR: Schneider V A; Mercola M  
CORPORATE SOURCE: Department of Cell Biology, Harvard Medical School, Boston,  
Massachusetts 02115, USA.  
CONTRACT NUMBER: RO1 HL59502 (NHLBI)  
SOURCE: Genes & development, (2001 Feb 1) 15 (3) 304-15.  
Journal code: 8711660. ISSN: 0890-9369.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200103  
ENTRY DATE: Entered STN: 20010404  
Last Updated on STN: 20010404  
Entered Medline: 20010315

L5 ANSWER 7 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 2001069917 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11044411  
TITLE: The role of Xenopus dickkopf1 in prechordal plate  
specification and neural patterning.  
AUTHOR: Kazanskaya O; Glinka A; Niehrs C  
CORPORATE SOURCE: Division of Molecular Embryology, Deutsches  
Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120  
Heidelberg, Germany.  
SOURCE: Development (Cambridge, England), (2000 Nov) 127 (22)  
4981-92.  
Journal code: 8701744. ISSN: 0950-1991.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200101  
ENTRY DATE: Entered STN: 20010322  
Last Updated on STN: 20010322  
Entered Medline: 20010104

=> d his

(FILE 'HOME' ENTERED AT 16:15:45 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 16:16:12 ON 25 JUL 2005

L1 446342 S BONE  
L2 133 S (DICKKOPF ()) 1) OR (DICKKOPF-1) OR DICKKOPF1 OR (DKK1) OR (DK  
L3 36 S L2 AND L1  
L4 12 S L3 NOT PY>2002  
L5 9 S L4 AND EXPRESS?

=> d ibib 8-9

L5 ANSWER 8 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 2000108581 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10640703  
TITLE: Requirement for anti-dorsalizing morphogenetic protein in  
organizer patterning.  
AUTHOR: Dosch R; Niehrs C  
CORPORATE SOURCE: Division of Molecular Embryology, Deutsches  
Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120,  
Heidelberg, Germany.  
SOURCE: Mechanisms of development, (2000 Feb) 90 (2) 195-203.  
Journal code: 9101218. ISSN: 0925-4773.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200004  
ENTRY DATE: Entered STN: 20000505  
Last Updated on STN: 20000505  
Entered Medline: 20000427

L5 ANSWER 9 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 1999425169 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10495270

TITLE: Dickkopf genes are co-ordinately expressed in mesodermal lineages.  
 AUTHOR: Monaghan A P; Kioschis P; Wu W; Zuniga A; Bock D; Poustka A; Delius H; Niehrs C  
 CORPORATE SOURCE: Division of Molecular Biology of the Cell I, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, D-69120, Heidelberg, Germany.  
 SOURCE: Mechanisms of development, (1999 Sep) 87 (1-2) 45-56.  
 Journal code: 9101218. ISSN: 0925-4773.  
 PUB. COUNTRY: Ireland  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-AJ243963; GENBANK-AJ243964  
 ENTRY MONTH: 200003  
 ENTRY DATE: Entered STN: 20000327  
 Last Updated on STN: 20000327  
 Entered Medline: 20000316

=> d 1-4

L5 ANSWER 1 OF 9 MEDLINE on STN  
 AN 2002693855 MEDLINE  
 DN PubMed ID: 12455632  
 TI Bmp, Fgf and Wnt signalling in programmed cell death and chondrogenesis during vertebrate limb development: the role of Dickkopf-1.  
 AU Grotewold Lars; Ruther Ulrich  
 CS Institut fur Entwicklungs- und Molekularbiologie der Tiere (EMT), Heinrich-Heine-Universitat, Dusseldorf, Germany.  
 SO International journal of developmental biology, (2002) 46 (7) 943-7.  
 Journal code: 8917470. ISSN: 0214-6282.  
 CY Spain  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200306  
 ED Entered STN: 20021214  
 Last Updated on STN: 20030619  
 Entered Medline: 20030618

L5 ANSWER 2 OF 9 MEDLINE on STN  
 AN 2002131765 MEDLINE  
 DN PubMed ID: 11867524  
 TI The Wnt antagonist Dickkopf-1 is regulated by Bmp signaling and c-Jun and modulates programmed cell death.  
 AU Grotewold Lars; Ruther Ulrich  
 CS Entwicklungs- und Molekularbiologie der Tiere, Heinrich-Heine Universitat, D-40225 Dusseldorf, Germany.. lars.grotewold@uni-duesseldorf.de  
 SO EMBO journal, (2002 Mar 1) 21 (5) 966-75.  
 Journal code: 8208664. ISSN: 0261-4189.  
 CY England: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200205  
 ED Entered STN: 20020228  
 Last Updated on STN: 20020515  
 Entered Medline: 20020514

L5 ANSWER 3 OF 9 MEDLINE on STN  
 AN 2001447406 MEDLINE  
 DN PubMed ID: 11291860  
 TI The role of the homeodomain protein Bozozok in zebrafish axis formation.



AU Solnica-Krezel L; Driever W  
 CS Department of Molecular Biology, Vanderbilt University, Nashville,  
 Tennessee 37235, USA.. lilianna.solnica-krezel@vanderbilt.edu  
 SO International journal of developmental biology, (2001) 45 (1) 299-310.  
 Journal code: 8917470. ISSN: 0214-6282.  
 CY Spain  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200108  
 ED Entered STN: 20010813  
 Last Updated on STN: 20010813  
 Entered Medline: 20010809

L5 ANSWER 4 OF 9 MEDLINE on STN  
 AN 2001447398 MEDLINE  
 DN PubMed ID: 11291852  
 TI Dickkopfl and the Spemann-Mangold head organizer.  
 AU Niehrs C; Kazanskaya O; Wu W; Glinka A  
 CS Division of Molecular Embryology, Deutsches Krebsforschungszentrum,  
 Heidelberg, Germany.  
 SO International journal of developmental biology, (2001) 45 (1) 237-40.  
 Ref: 34  
 Journal code: 8917470. ISSN: 0214-6282.  
 CY Spain  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Priority Journals  
 EM 200108  
 ED Entered STN: 20010813  
 Last Updated on STN: 20010813  
 Entered Medline: 20010809

=> d kwic 4

L5 ANSWER 4 OF 9 MEDLINE on STN  
 TI Dickkopfl and the Spemann-Mangold head organizer.  
 AB . . . the Spemann-Mangold organizer may be mediated by secreted Wnt  
 antagonists. Wnts are potent posteriorizing factors and antagonize the  
 Spemann-Mangold organizer. Dickkopfl (dkkl) encodes a  
 secreted effector expressed in head organizing centers of  
 Xenopus, mouse and zebrafish. It acts as a Wnt inhibitor and is able  
 together with. . . anteriorizes both mesendoderm and neuroectoderm,  
 promoting prechordal plate and forebrain fates. Injection of inhibitory  
 antibodies leads to microcephaly and cyclopia. Dkkl thus is an  
 essential mediator of the vertebrate head organizer.  
 CT Animals  
 Body Patterning  
 Bone Morphogenetic Proteins: AI, antagonists & inhibitors  
 Embryonic Induction  
 Head: EM, embryology  
 Mice  
 \*Organizers, Embryonic: PH, physiology  
 Proteins: GE, genetics  
 CN 0 (Bone Morphogenetic Proteins); 0 (Proteins); 0 (Proto-Oncogene  
 Proteins); 0 (Wnt proteins); 0 (Zebrafish Proteins); 0 (dkkl  
 protein, Xenopus); 0 (wnt8b protein, zebrafish)

=> d kwic 2

L5 ANSWER 2 OF 9 MEDLINE on STN

TI The Wnt antagonist Dickkopf-1 is regulated by Bmp signaling and c-Jun and modulates programmed cell death.

AB Dickkopf-1 (Dkk-1) has been shown to be a potent inhibitor of Wnt/beta-catenin signaling in a variety of assays and organisms. In this study, we show that expression of Dkk-1 overlaps significantly with the sites of programmed cell death in normal as well as mutant vertebrate limb development, and identify several of its upstream regulators, one of which is Bmp-4. Interestingly, Bmp-4 only activates Dkk-1 when it concomitantly induces apoptosis. Moreover, Dkk-1 is heavily up-regulated by UV irradiation and several other genotoxic stimuli. We further show that normal expression of Dkk-1 is dependent on the Ap-1 family member c-Jun and that overexpression of Dkk-1 enhances Bmp-triggered apoptosis in the vertebrate limb. Taken together, our results provide evidence for an important role of Dkk-1-mediated inhibition of Wnt/beta-catenin signaling in response to different stress signals that all converge on the activation of c-Jun in vivo.

CT Animals

Apoptosis: GE, genetics

Apoptosis: PH, physiology

Bone Morphogenetic Proteins: AI, antagonists & inhibitors

Bone Morphogenetic Proteins: PD, pharmacology

\*Bone Morphogenetic Proteins: PH, physiology

Chick Embryo

Cytoskeletal Proteins: AI, antagonists & inhibitors

DNA-Binding Proteins: BI, biosynthesis

DNA-Binding Proteins: GE, genetics

. . . Implants

Enzyme Inhibitors: PD, pharmacology

\*Extremities: EM, embryology

Fibroblast Growth Factors: PD, pharmacology

Fibroblasts: DE, drug effects

Fibroblasts: ME, metabolism

Gene Expression Regulation, Developmental: DE, drug effects

\*Gene Expression Regulation, Developmental: PH, physiology

Gene Expression Regulation, Developmental: RE, radiation effects

Mesoderm: ME, metabolism

Mice

Mice, Knockout

Morphogenesis

Protein Biosynthesis

Proteins: GE, genetics

Proteins: . . .

CN 0 (Bone Morphogenetic Proteins); 0 (Cytoskeletal Proteins); 0 (DNA-Binding Proteins); 0 (Drug Implants); 0 (Enzyme Inhibitors); 0 (Proteins); 0 (Proto-Oncogene Proteins); 0. . . 0 (Recombinant Fusion Proteins); 0 (Trans-Activators); 0 (Transcription Factor AP-1); 0 (Transcription Factors); 0 (Wnt proteins); 0 (Zebrafish Proteins); 0 (bone morphogenetic protein 4); 0 (dkk1 protein, Xenopus); 0 (hedgehog protein, vertebrate); 0 (lymphoid enhancer-binding factor 1); 0 (wnt8b protein, zebrafish)

=> d kwic 5

L5 ANSWER 5 OF 9 MEDLINE on STN

CT Animals

\*Blood Cells

Bone Morphogenetic Proteins: ME, metabolism

Ca(2+)-Calmodulin Dependent Protein Kinase: ME, metabolism

Central Nervous System: EM, embryology

Central Nervous System: ME, metabolism

Cytoskeletal Proteins: ME, metabolism

Drosophila: EM, embryology  
 Drosophila: ME, metabolism  
 \*Drosophila Proteins  
 \*Embryonic Induction  
 Endoderm: PH, physiology  
 Gene Expression Regulation, Developmental  
 Glycogen Synthase Kinase 3  
 \*Heart: EM, embryology  
 Hematopoiesis  
 Insect Proteins: ME, metabolism  
 Mesoderm: CY, cytology  
 Mesoderm: . . .  
 CN 0 (Bone Morphogenetic Proteins); 0 (Cytoskeletal Proteins); 0  
 (Drosophila Proteins); 0 (Insect Proteins); 0 (Proteins); 0  
 (Trans-Activators); 0 (Transcription Factors); 0 (Wnt-3 protein); 0  
 (Xenopus Proteins); 0 (crescent protein, Xenopus); 0 (dkk1  
 protein, Xenopus); 0 (dpp protein, Drosophila); 0 (wnt8a protein,  
 Zebrafish); EC 2.7.1.123 (Ca(2+)-Calmodulin Dependent Protein Kinase); EC  
 2.7.1.37 (Glycogen Synthase. . .

=> s osteo?

L6 211167 OSTEO?

=> d his

(FILE 'HOME' ENTERED AT 16:15:45 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 16:16:12 ON 25 JUL 2005

L1 446342 S BONE  
 L2 133 S (DICKKOPF () 1) OR (DICKKOPF-1) OR DICKKOPF1 OR (DKK1) OR (DK  
 L3 36 S L2 AND L1  
 L4 12 S L3 NOT PY>2002  
 L5 9 S L4 AND EXPRESS?  
 L6 211167 S OSTEO?

=> s 12 and 16

L7 24 L2 AND L6

=> s 15 not py>2002

1489868 PY>2002

L8 9 L5 NOT PY>2002

=> s 18 not py>2001

2029769 PY>2001

L9 7 L8 NOT PY>2001

=> d ibib 1-4

L9 ANSWER 1 OF 7 MEDLINE on STN  
 ACCESSION NUMBER: 2001447406 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11291860  
 TITLE: The role of the homeodomain protein Bozozok in zebrafish  
 axis formation.  
 AUTHOR: Solnica-Krezel L; Driever W  
 CORPORATE SOURCE: Department of Molecular Biology, Vanderbilt University,  
 Nashville, Tennessee 37235, USA.. lilianna.solnica-  
 krezel@vanderbilt.edu  
 SOURCE: International journal of developmental biology, (2001) 45  
 (1) 299-310.  
 Journal code: 8917470. ISSN: 0214-6282.  
 PUB. COUNTRY: Spain  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals

ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

L9 ANSWER 2 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2001447398 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11291852  
TITLE: Dickkopf1 and the Spemann-Mangold head organizer.  
AUTHOR: Niehrs C; Kazanskaya O; Wu W; Glinka A  
CORPORATE SOURCE: Division of Molecular Embryology, Deutsches  
Krebsforschungszentrum, Heidelberg, Germany.  
SOURCE: International journal of developmental biology, (2001) 45  
(1) 237-40. Ref: 34  
Journal code: 8917470. ISSN: 0214-6282.  
PUB. COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809

L9 ANSWER 3 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2001168646 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11269304  
TITLE: Development. The path to the heart and the road not taken.  
AUTHOR: Olson E N  
CORPORATE SOURCE: Department of Molecular Biology, University of Texas  
Southwestern Medical Center, Dallas, TX 75390, USA..  
eolson@hamon.swmed.edu  
SOURCE: Science, (2001 Mar 23) 291 (5512) 2327-8.  
Journal code: 0404511. ISSN: 0036-8075.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200104  
ENTRY DATE: Entered STN: 20010417  
Last Updated on STN: 20021218  
Entered Medline: 20010412

L9 ANSWER 4 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2001150174 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11159911  
TITLE: Wnt antagonism initiates cardiogenesis in *Xenopus laevis*.  
AUTHOR: Schneider V A; Mercola M  
CORPORATE SOURCE: Department of Cell Biology, Harvard Medical School, Boston,  
Massachusetts 02115, USA.  
CONTRACT NUMBER: R01 HL59502 (NHLBI)  
SOURCE: Genes & development, (2001 Feb 1) 15 (3) 304-15.  
Journal code: 8711660. ISSN: 0890-9369.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200103  
ENTRY DATE: Entered STN: 20010404  
Last Updated on STN: 20010404  
Entered Medline: 20010315

=> d kwic 2

L9 ANSWER 2 OF 7 MEDLINE on STN  
TI Dickkopf1 and the Spemann-Mangold head organizer.  
AB . . . the Spemann-Mangold organizer may be mediated by secreted Wnt antagonists. Wnts are potent posteriorizing factors and antagonize the Spemann-Mangold organizer. Dickkopf1 (dkk1) encodes a secreted effector expressed in head organizing centers of Xenopus, mouse and zebrafish. It acts as a Wnt inhibitor and is able together with. . . anteriorizes both mesendoderm and neuroectoderm, promoting prechordal plate and forebrain fates. Injection of inhibitory antibodies leads to microcephaly and cyclopia. Dkk1 thus is an essential mediator of the vertebrate head organizer.  
CT Animals  
Body Patterning  
Bone Morphogenetic Proteins: AI, antagonists & inhibitors  
Embryonic Induction  
Head: EM, embryology  
Mice  
\*Organizers, Embryonic: PH, physiology  
Proteins: GE, genetics  
CN 0 (Bone Morphogenetic Proteins); 0 (Proteins); 0 (Proto-Oncogene Proteins); 0 (Wnt proteins); 0 (Zebrafish Proteins); 0 (dkk1 protein, Xenopus); 0 (wnt8b protein, zebrafish)

=> d his

(FILE 'HOME' ENTERED AT 16:15:45 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 16:16:12 ON 25 JUL 2005

L1 446342 S BONE  
L2 133 S (DICKKOPF () 1) OR (DICKKOPF-1) OR DICKKOPF1 OR (DKK1) OR (DK  
L3 36 S L2 AND L1  
L4 12 S L3 NOT PY>2002  
L5 9 S L4 AND EXPRESS?  
L6 211167 S OSTEO?  
L7 24 S L2 AND L6  
L8 9 S L5 NOT PY>2002  
L9 7 S L8 NOT PY>2001

=> s 17 not py>2001

2029769 PY>2001

L10 0 L7 NOT PY>2001

=> s 17 not py>2002

1489868 PY>2002

L11 3 L7 NOT PY>2002

=> d ibib 1-3

L11 ANSWER 1 OF 3 MEDLINE on STN  
ACCESSION NUMBER: 2002280313 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12021176  
TITLE: Global gene profiling in human endometrium during the window of implantation.  
AUTHOR: Kao L C; Tulac S; Lobo S; Imani B; Yang J P; Germeyer A; Osteen K; Taylor R N; Lessey B A; Giudice L C  
CORPORATE SOURCE: Department of Gynecology and Obstetrics, Stanford University, Stanford, California 94305, USA.  
CONTRACT NUMBER: U54 HD31398 (NICHD)  
SOURCE: Endocrinology, (2002 Jun) 143 (6) 2119-38.  
Journal code: 0375040. ISSN: 0013-7227.  
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200206  
ENTRY DATE: Entered STN: 20020522  
Last Updated on STN: 20020619  
Entered Medline: 20020618

L11 ANSWER 2 OF 3 MEDLINE on STN  
ACCESSION NUMBER: 2002275003 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12015398  
TITLE: Regulation of bone formation and vision by LRP5.  
COMMENT: Comment on: N Engl J Med. 2002 May 16;346(20):1513-21.  
PubMed ID: 12015390  
AUTHOR: Patel Millan S; Karsenty Gerard  
SOURCE: New England journal of medicine, (2002 May 16) 346 (20)  
1572-4.  
Journal code: 0255562. ISSN: 1533-4406.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Commentary  
Editorial  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Space  
Life Sciences  
ENTRY MONTH: 200205  
ENTRY DATE: Entered STN: 20020517  
Last Updated on STN: 20020623  
Entered Medline: 20020522

L11 ANSWER 3 OF 3 MEDLINE on STN  
ACCESSION NUMBER: 2002274995 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12015390  
TITLE: High bone density due to a mutation in LDL-receptor-related  
protein 5.  
COMMENT: Comment in: N Engl J Med. 2002 May 16;346(20):1572-4.  
PubMed ID: 12015398  
Comment in: N Engl J Med. 2002 Sep 19;347(12):943-4; author  
reply 943-4. PubMed ID: 12239268  
Comment in: N Engl J Med. 2002 Sep 19;347(12):943-4; author  
reply 943-4. PubMed ID: 12240686  
Comment in: N Engl J Med. 2004 May 13;350(20):2096-9;  
author reply 2096-9. PubMed ID: 15141052  
AUTHOR: Boyden Lynn M; Mao Junhao; Belsky Joseph; Mitzner Lyle;  
Farhi Anita; Mitnick Mary A; Wu Dianqing; Insogna Karl;  
Lifton Richard P  
CORPORATE SOURCE: Department of Genetics, Yale University School of Medicine,  
New Haven, Connecticut 06510, USA.  
CONTRACT NUMBER: AG15345 (NIA)  
AR46032 (NIAMS)  
CA85420 (NCI)  
RR00125 (NCRR)  
SOURCE: New England journal of medicine, (2002 May 16) 346 (20)  
1513-21.  
Journal code: 0255562. ISSN: 1533-4406.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 200205  
ENTRY DATE: Entered STN: 20020517  
Last Updated on STN: 20020926  
Entered Medline: 20020522

=> d kwic 3

L11 ANSWER 3 OF 3 MEDLINE on STN

AB BACKGROUND: Osteoporosis is a major public health problem of largely unknown cause. Loss-of-function mutations in the gene for low-density lipoprotein receptor-related protein 5 (LRP5), which acts in the Wnt signaling pathway, have been shown to cause osteoporosis -pseudoglioma. METHODS: We performed genetic and biochemical analyses of a kindred with an autosomal dominant syndrome characterized by high bone density,. . . flies to humans. Markers of bone resorption were normal in the affected subjects, whereas markers of bone formation such as osteocalcin were markedly elevated. Levels of fibronectin, a known target of signaling by Wnt, a developmental protein, were also elevated. In vitro studies showed that the normal inhibition of Wnt signaling by another protein, Dickkopf-1 (Dkk -1), was defective in the presence of LRP5V171 and that this resulted in increased signaling due to unopposed Wnt activity. CONCLUSIONS:. . . LRP5 function in high bone mass and point to Dkk as a potential target for the prevention or treatment of osteoporosis

CT

GE, genetics

Case-Control Studies

Chromosomes, Human, Pair 11

Genes, Dominant

Genotype

Humans

Mandible: PA, pathology

Mandible: RA, radiography

Mutation, Missense

Osteogenesis: PH, physiology

Palate: PA, pathology

Pedigree

\*Point Mutation

Proteins: PD, pharmacology

Proto-Oncogene Proteins: AI, antagonists & inhibitors

\*Proto-Oncogene Proteins:. . .

CN 0 (Biological Markers); 0 (Proteins); 0 (Proto-Oncogene Proteins); 0 (Receptors, LDL); 0 (Wnt proteins); 0 (Zebrafish Proteins); 0 (dkkl protein, Xenopus); 0 (lipoprotein receptor related protein 5); 0 (wnt8b protein, zebrafish)

=> d his

(FILE 'HOME' ENTERED AT 16:15:45 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 16:16:12 ON 25 JUL 2005

L1 446342 S BONE  
L2 133 S (DICKKOPF () 1) OR (DICKKOPF-1) OR DICKKOPF1 OR (DKK1) OR (DK  
L3 36 S L2 AND L1  
L4 12 S L3 NOT PY>2002  
L5 9 S L4 AND EXPRESS?  
L6 211167 S OSTEO?  
L7 24 S L2 AND L6  
L8 9 S L5 NOT PY>2002  
L9 7 S L8 NOT PY>2001  
L10 0 S L7 NOT PY>2001  
L11 3 S L7 NOT PY>2002

=> s lesion

141659 LESION

302187 LESIONS

L12 391994 LESION

(LESION OR LESIONS)

=> s l12 and l2  
L13 5 L12 AND L2  
  
=> s l13 not py>2002  
1489868 PY>2002  
L14 0 L13 NOT PY>2002  
  
=> d his

(FILE 'HOME' ENTERED AT 16:15:45 ON 25 JUL 2005)

FILE 'MEDLINE' ENTERED AT 16:16:12 ON 25 JUL 2005

L1 446342 S BONE  
L2 133 S (DICKKOPF () 1) OR (DICKKOPF-1) OR DICKKOPF1 OR (DKK1) OR (DK  
L3 36 S L2 AND L1  
L4 12 S L3 NOT PY>2002  
L5 9 S L4 AND EXPRESS?  
L6 211167 S OSTEO?  
L7 24 S L2 AND L6  
L8 9 S L5 NOT PY>2002  
L9 7 S L8 NOT PY>2001  
L10 0 S L7 NOT PY>2001  
L11 3 S L7 NOT PY>2002  
L12 391994 S LESION  
L13 5 S L12 AND L2  
L14 0 S L13 NOT PY>2002

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

10.06

10.27

STN INTERNATIONAL LOGOFF AT 16:26:32 ON 25 JUL 2005